Hospital Library
610.5
A671
S961

VOLUME 22 NUMBER 3

ARCHIVES OF SURGERY

EDITORIAL BOARD

DEAN LEWIS, Baltimore

EVARTS A. GRAHAM, St. Louis
WALLACE I. TERRY, San Francisco
HUGH CABOT, Rochester, Minn.
WILLIAM DARRACH, New York
EDWARD STARR JUDD, Rochester, Minn.

MARCH, 1931

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second-Class Matter, July 10, 1925, at the Postoffice at Chicago, Illinois, Under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of Oct. 3, 1917, authorized July 29, 1920.

CONTENTS OF PREVIOUS NUMBER

FEBRUARY, 1931. NUMBER 2

Diabetic Gangrene: Medical Treatment and Prophylaxis. Howard F. Root, M.D., Boston.

Explosions Occurring During the Use of Ethylene. Franklin D. Johnston, B.S. (Eng.), M.D., Ann Arbor, Mich., and Hugh Cabot, M.D., Rochester, Minn.

The Volume of Blood Flow per Minute Through the Lungs Following Collapse of One Lung by Occlusion of Its Bronchus: Experimental Observations. Richmond L. Moore, M.D., New York.

Multiple Neurofibromatosis (von Recklinghausen's Disease), with Special Reference to Malignant Transformation. Kiyoshi Hosoi, M.D., Albany, N. Y.

Congenital Deficiency of the Pericardium: The Function of the Pericardium. Claude S. Beck, M.D., Cleveland.

Thoracoplasty as a Method of Treatment in Pulmonary Tuberculosis: Report of Fifty-Three Cases. B. N. Carter, M.D., Cincinnati.

Actinomycosis of the Abdomen. Louis P. Good, M.D., Rochester, Minn.

Trauma to the Intestines: The Importance of the Local Loss of Fluid in the Production of Low Blood Pressure. Alfred Blalock, M.D., Nashville, Tenn.

Forty-Third Report of Progress in Orthopedic Surgery. Philip D. Wilson, M.D.; Lloyd T. Brown, M.D.; M. N. Smith-Petersen, M.D.; John G. Kuhns, M.D., and Edwin F. Cave, M.D., Boston; Ralph K. Ghormley, M.D., Rochester, Minn.; Murray S. Danforth, M.D., Providence, R. I.; George Perkins, London, England; Arthur Van Dessel, M.D., Louvain, Belgium, and C. Hermann Bucholz, M.D., Halle, Germany.

COPYRIGHT, 1931, BY THE AMERICAN MEDICAL ASSOCIATION

ARCHIVES OF SURGERY

VOLUME 22 MARCH, 1931 NUMBER 3

RECURRENCE OF VARICOSE VEINS FOLLOWING INJECTION

A STUDY OF THE PATHOLOGIC NATURE OF THE RECURRENCE AND A CRITICAL SURVEY OF THE INJECTION METHOD *

NELSON J. HOWARD, M.D.

C. R. JACKSON, A.B.

AND

EDMUND J. MAHON, M.D.

SAN FRANCISCO

A study of the end-results of our treatment of varicose veins by the injection method during the past three years has revealed a startling percentage of recurrences. In a small series of sixty-six cases, recurrence has been observed a year or more after thrombosis in fifty-two patients. These results are in such contrast to the enthusiastic reports of the treatment of varicose veins by injection that a critical review of the therapeutic thrombosis of varicose veins seems justified. The wave of enthusiasm that several years ago greeted the treatment of varicose veins by the injection of sclerosing agents gave the method an impetus that has not been justified by the ultimate results, and it is becoming increasingly evident that a more careful elimination of unsuitable cases and a return to surgical procedures combined with injection of sclerosing agents is necessary to obtain satisfactory and more permanent results.

METHOD

The treatment of these patients was begun in November, 1927, at the suggestion of Dr. Emile Holman, in an effort to compare this method with the results known to be obtained by operation. A careful history was obtained in each case and a general physical examination made, with records of blood pressure, urinalysis, leukocyte counts and Wassermann tests. In addition, before beginning treatment a careful history of factors related to varicose veins was obtained on a special blank form, and the position of the varices, ulcer and areas of eczema recorded on a special graphic chart. These charts were a modification of those suggested by Nicholson.[1] The patients were examined also

* Submitted for publication, May 5, 1930.

* From the Department of Surgery, Stanford University Medical School.

1. Nicholson, B. B.: Varicose Veins; Etiology and Treatment: A Clinical and Histologic Study, Arch. Surg. **15**:351 (Sept.) 1927.

by the usual Trendelenburg procedure to test the competency of the saphenous and perforating valves, and by the tourniquet constriction walking test, or by the use of pressure bandages over a period of from two to four days, to test the patency of the deep veins.

A 20 per cent solution of sodium chloride has been used as the sclerosing agent in the treatment of these sixty-six patients. It was found convenient to enter the veins with the patient standing, while the injection was made in the supine or sitting position with the legs elevated. Various procedures for promoting thrombosis were utilized, such as "stripping" the vein with the finger proximal to the point of injection, the application of the tourniquet, the use of hot 20 per cent saline solution at from 105 to 110 F., and massage about the site of injection following withdrawal of the needle. Pressure bandages were used for at least two weeks after thrombosis in an endeavor to obtain collapse of the veins with agglutination and organization of the wall of the collapsed vein. In the beginning, patients were admitted to the hospital wards and were given injections at intervals of from one to two days. Forty-three patients were treated in the hospital. After becoming familiar with the technical difficulties and the dangers of the new method and convinced that satisfactory thrombosis could be easily produced, ambulatory treatment of the patients was begun. The patients were as thoroughly examined as in the hospital admissions, and one afternoon a week was devoted to the ambulatory treatment. Patients were treated once a week. From one to three injections were given at a sitting and from 10 to 12 cc. of the sodium chloride solution at a single injection.

With the method described, thrombosis of varicose veins was easily obtained. A few cases were at first refractile to the treatment, and thrombosis was secured by injection of 30 per cent dextrose, quinine and urethane, or by repeated injections of salt. Complete thrombosis was obtained in forty-eight cases. One patient had varicose veins remaining after the excision of a femoral arteriovenous fistula, and in this instance complete thrombosis was not thought desirable. In several of the early patients incomplete thrombosis was obtained because of our unfamiliarity with the method. The remainder of the eighteen patients in whom thrombosis was incomplete represent patients who stopped treatment and those who had such large varicosities with ulceration, hard brawny edema of the leg and completely incompetent valves that although the greater number of veins were thrombosed, the older thrombi recanalized or were absorbed before injections were complete. These last patients are still being treated.

Injections were considered complete when all visible and palpable veins with the exception of small telangiectases were thrombosed. Thrombosis of the internal saphenous in the thigh was attempted even

if the vein was not dilated or visible. Many of the patients showed thrombosis of the saphenous veins up to the saphenous bulb at the entrance into the femoral vein. Complete thrombosis was obtained in forty-eight patients, 72 per cent of the cases. A few of the eighteen patients classed as having incomplete thrombosis had one or two isolated veins or perforating veins still patent, although the remaining veins were well thrombosed.

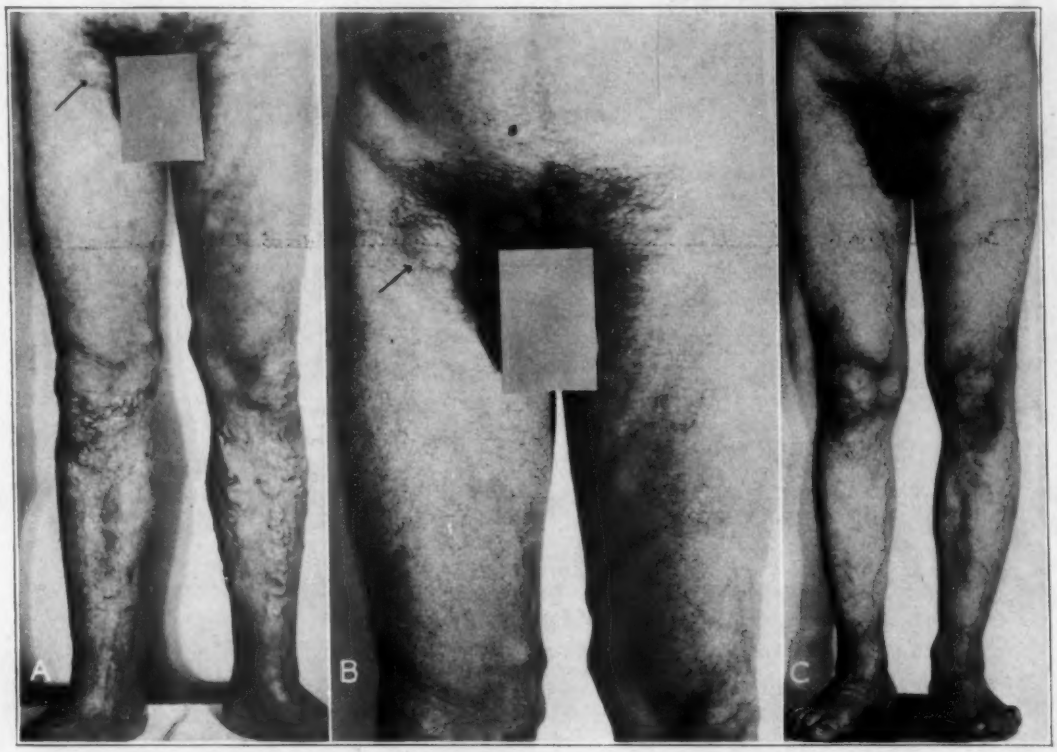


Fig. 1.—*A* shows the patient before injection, with marked bilateral varicose veins, incompetent saphenous and perforating veins and dilated saphenous bulbs in both groins. In *B* the arrow points to the dilated saphenous bulb. *C* shows the result from reinjection after complete recurrence.

One outstanding example was a patient in whom the entire saphenous system was dilated, with large, tortuous veins below the knee, and very prominent saphenous bulbs (fig. 1). Twice the patient had been told by physicians that he had bilateral femoral hernias, and was advised to submit to operation. A third physician had prescribed a double truss, which the patient wore over the saphenous bulbs for some months with discomfort. In this man complete thrombosis of all veins

of the saphenous system of both legs was obtained, yet these same varicosities recurred within eight months after thrombosis. Injection was repeated with equally satisfactory immediate results, and within four months the saphenous vein on the right had recanalized to below the knee with beginning recurrence in the varicosities of the left leg. It is only because of the completeness of the thrombosis obtained in these cases that we have the temerity to report such a high percentage of recurrences, and to feel that the fault is not in the method or in the solution used, but in the natural reparative processes of the body.

A comparison between the patients treated by injection every one or two days and the patients receiving weekly treatments shows the average number of injections to be four per patient for the patients in the ward, while the average number of injections for the ambulatory outpatient series was eight. Satisfactory thrombosis was secured in an average of four and one-half days in the hospital series, while patients coming to the outpatient department were under treatment for an average of 6.6 weeks. Thus it is evident that private patients may have their veins thrombosed easily within a week by daily injection, and it suggests that an outpatient varicose vein clinic would be managed to a better advantage as a daily clinic.

RECURRENCES

Patients in whom complete thrombosis was obtained were asked to report back in three months, six months and a year. They were prompt about keeping the appointment after three months, but the majority did not appear after six months or a year. It was noticed that those who did return after six months showed beginning or complete recurrence. In December, 1929, we made a definite, organized attempt to see and examine all patients whose veins had been thrombosed by injection a year or more before. In the follow-up studies, seventeen of the sixty-six patients could not be located. It was known from the records that four of the seventeen had early recurrences. One patient was seen nine months after completion of treatment with firm thrombosis and without recurrence, and this patient is classed with those followed for a year or more. In the remaining forty-eight patients recurrence was demonstrated in every case. The actual recurrence rate, then, is 79 per cent of all patients, or 98 per cent of those followed for a year or more. The average time of observance of recurrence was ten and one-half months. The shortest period before observation of recurrence is three months and the longest twenty-four months. Collapse and adherence of the walls of the vein occurred in only three cases, and in these the collapse affected only segments of the vein.

It is of interest that in patients who had competent valves of the perforating set but incompetent valves of the saphenous vein recurrences

developed with as great a regularity and within the same space of time as in those who had incompetent valves in both perforating and saphenous veins.

The one person who had a satisfactory and complete thrombosis happened to have a single dilated straight saphenous vein in the right calf with competent saphenous and perforating valves. This man was seen nine months after thrombosis but cannot be located now.

COMPLICATIONS

Mention should be made of the complications encountered in this series. Perivenitis, apparently more alarming and painful than dangerous, occurred in eighteen cases. Rest in bed with compresses and elevation of the legs brought relief, but the process often lasted from three to four weeks before completely subsiding. Sloughs were produced by perivenous injection or leakage along the needle track in eleven cases. All but one of these were small. Separation of the slough took place in from three to four weeks, and for complete healing from eight to ten weeks were necessary. Definite nonfatal pulmonary embolism with frothy, bloody expectoration, pleural pain, physical and roentgenographic signs of consolidation of one lobe of the lung occurred in one person. A second patient, whose case report follows, received four injections, and a slough resulted at one point from extravasation into the tissues.

At the time of this patient's admission to the hospital physical examination revealed enlarged, reddened tonsils and an injected pharynx. The white blood count was 17,750. She was discharged from the hospital and requested to return in one month for tonsillectomy. She lived at a distance of ninety miles, and instructions were given as to the care of the slough. She returned in one month with the story that she had had severe sore throat for one week with slight substernal pain, an unproductive cough and tenderness and swelling of the right wrist. The day of readmission to the hospital she suddenly became short of breath, with palpitation and very rapid heart beat. Physical examination showed that she was acutely ill and dyspneic, and that there was marked heaving of the precordium that could be seen through the bed clothes. Her throat was intensely injected. There was dulness of the upper lobe of the right lung with suppression of the breath sounds. The heart was enlarged to the left. The extremities were normal, except for the irregular ulcer on the left shin, which had a sloughing base. The urine was normal when examined. The white blood count was 28,000 with 95 per cent polymorphonuclear leukocytes. The temperature was 38 C. (100.4 F.), the pulse rate 160 and the respirations 50 per minute. The patient's condition remained the same to the fourth day after admission, when she began to cough up bloody, frothy material. Over the upper part of the right side of the chest there appeared bronchovesicular breathing and an increased transmission of voice sounds to ausculation. The blood culture showed no growth. A culture from the throat showed streptococci of the green pigment-producing type with nonhemolytic streptococci. Culture of the ulcer on the leg showed *Bacillus coli*. The patient died of cardiac failure on the fifth day after admission. Autopsy could

not be obtained. The final hospital diagnosis was sepsis, acute follicular tonsillitis and pharyngitis, ulcer of the leg, acute endocarditis and questionable pulmonary infarct.

SYMPTOMATIC RELIEF

It is interesting to contrast the symptoms before and after injection. Such a comparison gives a more optimistic picture of the value of therapeutic thrombosis of varicose veins. Sixty-four of sixty-six patients complained of symptoms other than the presence of unsightly veins. Thirty-five complained of burning pains in the course of the veins. Fifty-eight suffered from pain and fatigue in the legs when working or while standing for hours. Spontaneous hemorrhages had occurred in five persons. Ulceration had occurred in twenty-six cases, and in three people there were ulcers on both legs. Swelling of the ankles at the end of the day was experienced by forty-eight patients, and eczema of the legs was an added burden in sixteen.

Symptomatic relief lasting a year or more occurred in forty-nine patients of whom we have definite records. Eight of these patients still had pain, ten experienced fatigue of the calf muscles when standing for hours, and four patients had itching of the legs. In six patients, ulcers had recurred. One person still suffered occasional cramps in the leg. In thirty-seven patients, the veins were visible as definite large varicosities, and in fifty-two, it was possible to determine by palpation that the lumen of the veins was patent and to demonstrate a transmitted impulse in the recurrent veins by tapping with the finger on the saphenous vein in the thigh.

Complete relief from symptoms was obtained in twenty-eight, and partial or complete relief in forty-nine of fifty-two patients. Many of the patients were greatly surprised when asked to return for reinjection or operative excision of the recurrent veins. We do not feel that this relative freedom from symptoms is a guarantee against progressive enlargement of the recurrent veins or the usual varicose complications of ulcer, eczema or edema.

MICROSCOPIC STUDY OF INJECTED VEINS

Efforts to obtain permission from our patients to excise segments of thrombosed veins under local anesthesia did not meet with much success, and the material was supplemented with excised segments of thrombosed veins secured by Dr. E. J. Mahon from the U. S. Marine Hospital, San Francisco. Microscopic paraffin sections were utilized in the study to determine the process of thrombosis and recurrence.

Thrombosis of the veins, except as noted, was obtained by injection of 20 per cent sodium chloride, and all of the veins selected for microscopic examination were found to be firm and hard within twenty-four hours after injection.

Fig. 2.—Low power photomicrograph taken forty-eight hours after injection. The lumen of the vessel is filled with a red thrombus; leukocytic infiltration is progressing. This and the following photomicrographs were supplied by Dr. Frank E. Blaisdell.

Twenty-four hours after injection, the vein was palpated as a firm, hard, slightly tender cord, and gave no impulse on percussion. Microscopic sections showed the lumen of the vein to be filled with a red thrombus composed of closely packed red blood cells with areas of hyaline bluish lines of Zahn. The intima was partially destroyed, and the regularly spaced endothelial cells were visible only in small portions of the vein. Fine tiny threads of fibrin reached out from the wall of

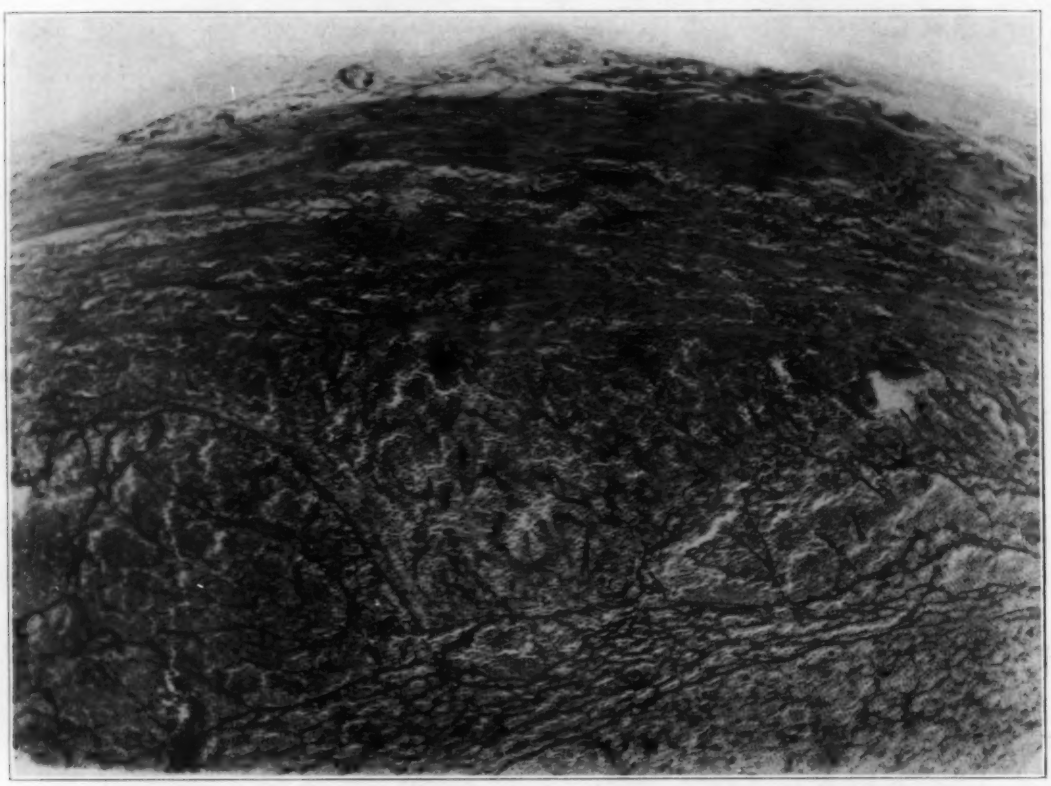


Fig. 3.—High power photomicrograph taken seventy-two hours after injection. The fibrin network is rendered distinct by agglutination of pigment granules along the fibrin threads. Spliting of the vessel wall is shown, with a beginning ingrowth of endothelial cells.

the vein into the thrombus. The vasa vasorum were engorged and there was edema of the adventitia and perivascular tissues.

Forty-eight hours after injection, the sections showed essentially the same picture as the twenty-four hour specimen; the red cells were collected into large, irregular, homogeneous groups, the cell outlines being indistinct, and innumerable fine pigment granules were seen

throughout the thrombus which tended to collect about white cells, the fibrin threads and the lines of Zahn (fig. 2).

Seventy-two hours after injection, the fibrin network of the thrombus was made more distinct by the collection along the fibrin strands of the pigment granules (fig. 3). Phagocytic cells were invading the thrombus and an occasional invading endothelial cell could be made out near the periphery of the thrombus. The vasa vasorum showed swell-

Fig. 4.—Low power photomicrograph taken six days after thrombosis. Cleavage spaces at the periphery are lined with endothelium and contain fresh blood. The arrows point to cleavage space and new vessels.

ing and proliferation of their endothelial cells, the lining of the vessels almost resembling cuboidal epithelium.

Six days after injection, the thrombus showed the red cells to be in homogeneous masses with indistinct cell outlines. Leukocytic infiltration of the thrombus was well advanced, and the pigment granules were found in larger masses within the phagocytic cells. Cleavage spaces had appeared between the thrombus and the wall of the vessel and were filled with fresh red blood cells (fig. 4).

Nine days after thrombosis, the vasa vasorum were markedly engorged and distended. The red thrombus filling the lumen had retracted from the wall of the vessel, leaving two large, crescentic, lacunar-like spaces between the thrombus and the vessel wall which were lined with endothelium and filled with fresh blood. The two broad points of attachment of the thrombus to the wall of the vessel showed

Fig. 5.—Low power photomicrograph taken three weeks after thrombosis. There is a peripheral zone of organization with new blood vessels, fibroblasts and a central zone of unorganized thrombus with apparent softening. Such softening may lead to opening up of considerable lumen by absorption of the softened thrombus (Welch). The arrows point to new lacunar vascular sinuses lined with endothelium and containing fresh blood.

an advancing invasion of numerous tiny capillaries and endothelial cells along the fibrin strands into the thrombus.

Thirteen days after thrombosis, the thrombus was still composed mainly of hyaline homogeneous masses of red blood cells with faint

outlines, and leukocytes caught in the fibrin network. The thrombus had separated from the vessel wall along two thirds of its circumference and remained attached by a broad pedicle. The lacunar space formed by this separation was filled with fresh blood and lined with endothelium, and new capillary vessels were growing from the endothelial lining of the space and from the broad pedicle of the thrombus out into the fibrin network. The proliferation of fibroblasts was advancing with

Fig. 6.—High power photomicrograph taken three weeks after thrombosis. Organization is proceeding from the old intima. Large spaces are seen lined with endothelium and containing fresh blood.

the new capillary vessels. Many of the new blood vessels were relatively large and all contained fresh blood cells.

Three weeks after thrombosis, the center of the thrombus was still composed of masses of hyaline, faintly staining red blood cells. There were fairly large lacunar spaces at the periphery of the thrombus, lined with endothelium and filled with fresh blood. The new vessels growing from the intimal surface of the vessel penetrated for some distance into the thrombus and were accompanied by fibroblasts (figs. 5 and 6).

Five weeks after thrombosis, the thrombus was invaded from almost all portions of the intimal surface of the lumen by small capillary vessels. Fibroblastic proliferation had taken place and for over half the circumference of the wall of the vessel definite organization had advanced a short distance into the thrombus. A bridge of organized fibroblastic

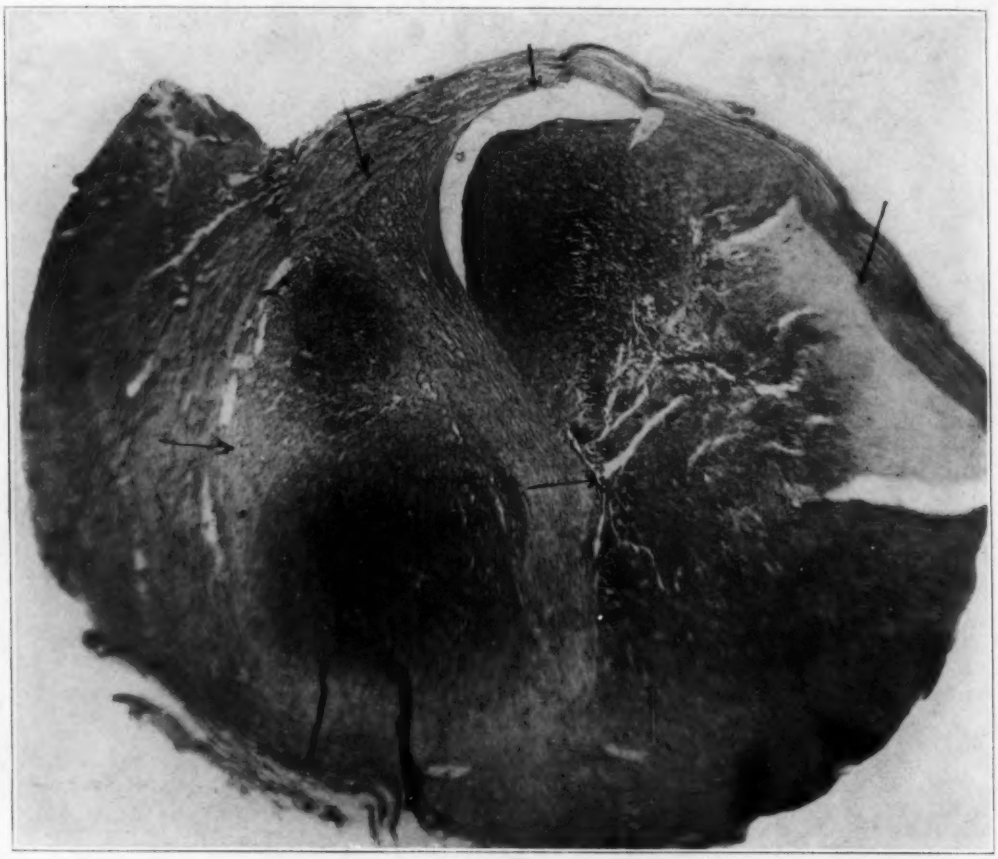


Fig. 7.—Low power photomicrograph taken five weeks after thrombosis. Partial organization is seen advancing from the periphery and from the organized vascular fibrous bridge. There is a small central "Y" shaped lumen lined with endothelium. One large lacunar endothelial lined space is seen. To the left the unorganized thrombus shows signs of apparent softening.

tissue with numerous small blood vessels bisected the lumen of the vessel (figs. 7 and 8).

Eight weeks after thrombosis, complete organization had taken place. The site of the previous intimal coat was marked by newly formed tissue

Fig. 8.—High power photomicrograph taken five weeks after thrombosis. The vascular fibrous bridge, the lacunar endothelial lined space, and organization advancing from the old intima into the thrombus are shown.

composed of small capillary vessels, large blood vessels that formed distinct vascular sinuses, and by a marked invasion and proliferation of fibroblasts. Although organization was almost complete, there was an

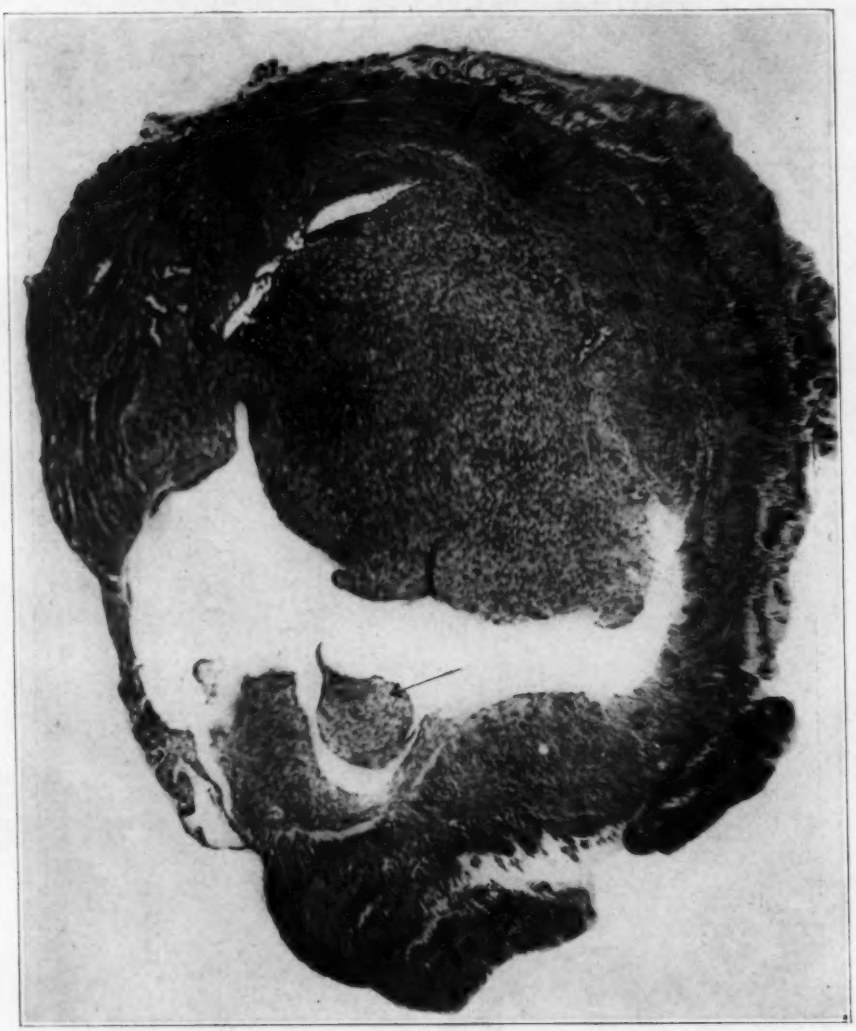


Fig. 9.—Low power photomicrograph taken eight weeks after thrombosis. The lumen is reestablished and the remains of the thrombus are seen as an organized mural thrombus with one small pedunculated mural thrombus.

irregular lumen about one-third the size of the original lumen; it was lined with endothelium, and its walls were formed by the fibrous granulation tissue of the organized thrombus (fig. 9). A pedunculated mural thrombus could be seen.

Eight weeks after thrombosis, the fatty tissue about the adventitia had areas of dense perivascular round cell infiltration. The muscularis of the media had numerous small blood vessels penetrating the circular muscle in an oblique direction. The old intimal margin marked the beginning of a vascular granulation tissue. Numerous blood spaces lined with endothelium and containing fresh blood had appeared. One

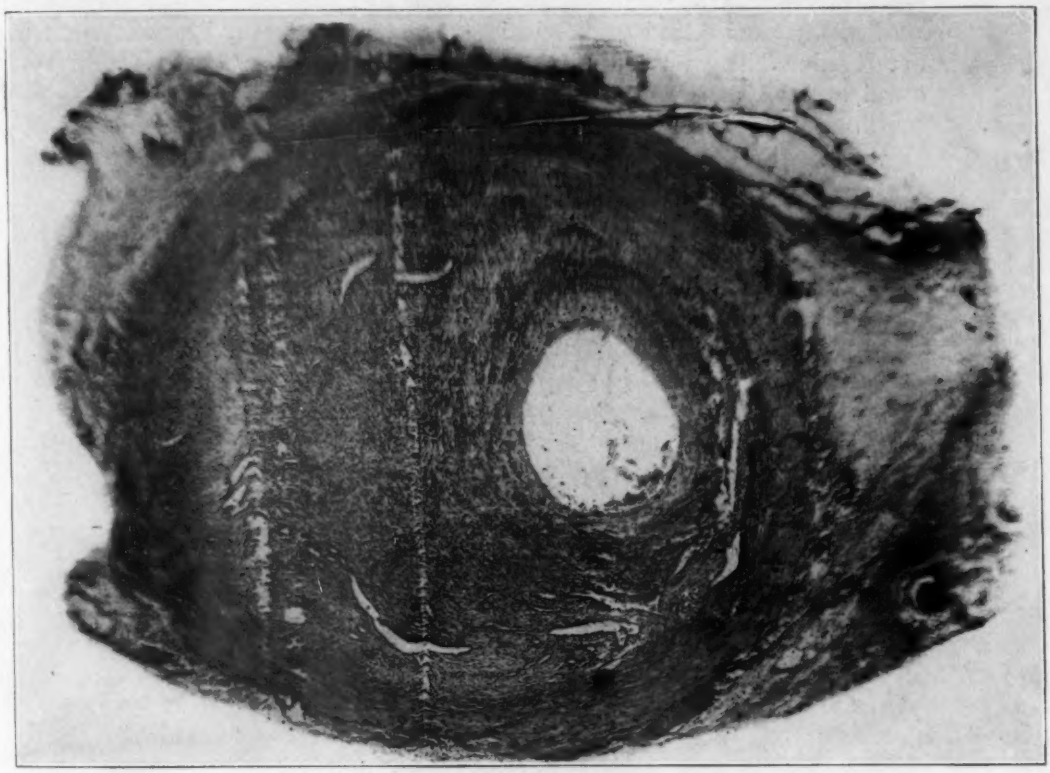


Fig. 10.—Low power photomicrograph taken eight weeks after thrombosis. Almost complete organization of thrombus by highly vascular tissue is seen. Sinuses and lacunar spaces are seen. A large eccentric lumen is lined with endothelium, contains fresh blood, and apparently was formed by absorption of a softened portion of the thrombus.

large circular blood space, a fifth of the size of the old lumen, was patent (fig. 10).

Three and one-half months following thrombosis with sodium chloride 30 per cent and dextrose 50 per cent, there was a proliferative endovenitis concentrically narrowing the vessel lumen by about one-fifth. The remaining four fifths of the lumen contained fresh red

blood cells. There was a definite laying down of fibrous tissue along the delicate new blood vessels, and fresh red blood cells were found between the meshes of the fibrovascular tissue. There was a marked perivenitis with pronounced perivascular round cell infiltration in the adventitia and surrounding fat (fig. 11).

Four and one-half months following thrombosis with 30 per cent sodium chloride and 50 per cent dextrose, the adventitia showed a moderate perivenitis. The lumen of the vessel showed fibrosing endovenitis with scanty small blood vessels which narrowed the lumen by about one-fourth. There was one pedunculated mural thrombus fixed by a broad base which showed partial organization. The remaining three fourths of the vessel lumen was patent and contained fresh blood (fig. 12).

Nine months after injection with sodium salicylate, complete organization and fibrosis of the thrombus had occurred. The strands of fibrous tissue and nuclei were arranged in a radial direction from the center of the lumen, and only small blood vessel sinuses were seen, with a tiny central lumen. This patient had had three operations for varicose veins, and the vessel thrombosed by injection was a single, isolated vessel running between the scars of previous operations.

Ten months after thrombosis with 20 per cent sodium chloride, the wall of the vessel still showed the site of the old intima marked by the beginning of a dense fibrous tissue with the fibrin bundles and nuclei pointing toward the lumen. At the junction of the old intima and the fibrous tissue, there were numerous vessels and small blood sinuses. A good sized lumen, about one third of the old lumen in caliber, was lined with endothelium (fig. 13).

REPORTED RECURRENCES

In the extensive literature on the treatment of varicose veins by injection, most authors have directed their attention to the method of accomplishing the thrombosis, the solution advocated and the question of embolism. Scant notice has been given to end-results, and few studies are available. P. Linser [2] and Zirn,[3] in reporting the results obtained at Linser's clinic, from 1916 to 1925, in over 1,300 cases following the injection of mercuric chloride, do not present a follow-up

2. Linser, P.: Ueber die konservative Behandlung der Varicen, Med. Klin. **12**:897, 1916; Die Behandlung der Krampfadern mit Sublimateinspritzungen und ihre Erfolge, ibid. **17**:1445, 1921; Die Behandlung der Varizen mit künstliche Thrombosierung, Dermat. Ztschr. **45**:22, 1925.

3. Zirn, Camillo: Die Behandlung der Krampfadern mit intravenösen Sublimatinjektionen, Dermat. Ztschr. **23**:650, 1916; München. med. Wchnschr. **66**: 382, 1919.

Fig. 11.—Low power photomicrograph taken three and one-half months after thrombosis. The vessel lumen is narrowed by an organized vascular mural thrombus. The lumen is patent and contains fresh blood.

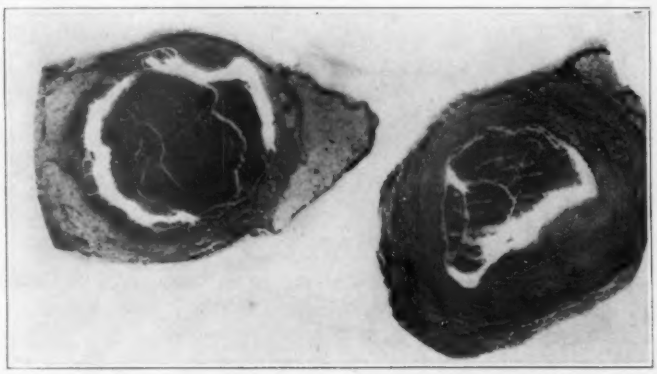


Fig. 12.—Low power photomicrograph. There is an organized vascular mural thrombus narrowing the vessel lumen.

study of their cases. They mentioned that they have many early cases in which the patients are free from complaints for several years and are able to work, and that from three to four years after injection the patients may show recurrence in collaterals in the veins that have not been treated, but that the treated veins have disappeared or are palpable

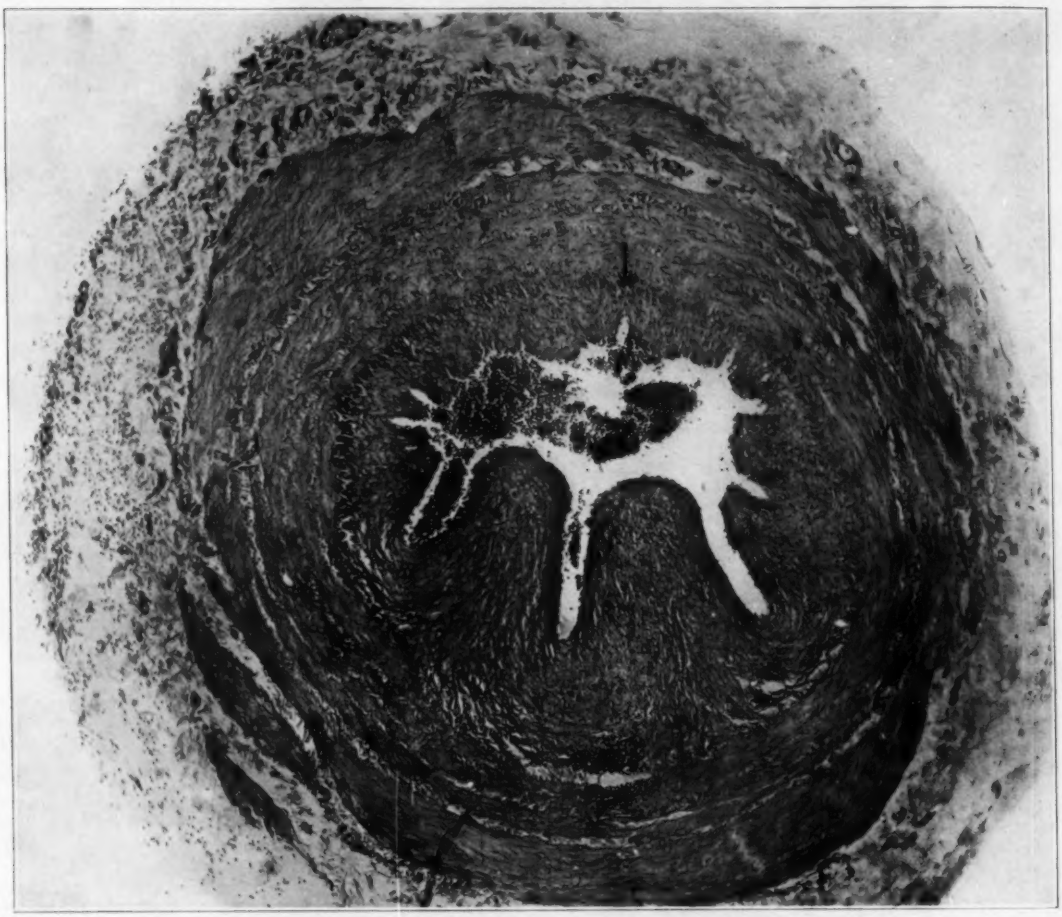


Fig. 13.—Low power photomicrograph taken ten months after thrombosis. The site of the old intima marks the origin of an irregularly festooned mural thrombus. The organized thrombus still contains numerous blood vessels.

as thin cords. K. Linser,[4] after two years' experience with sodium chloride, did not mention recurrences and presented no survey of the

4. Linser, K.: Zur Behandlung der Varizen mit Intravenösen Injektionen, München. med. Wchnschr. **71**:515, 1924; Die Behandlung der Krampfadern mit intravarikosen Kochsalzinjektionen, Dermat. Wchnschr. **81**:1345, 1925.

final results. Hemple [5] expressed the belief that not sufficient time has elapsed to judge of the permanency of the results and stated that collaterals developed in 12 per cent of his cases. Fischer,[6] who used mercuric chloride, had a number of patients in whom for from three to five years after treatment one was able to feel thrombosed cords, and who were free from symptoms. He gives no statistics as to permanency of results. Using calorose, an invert sugar, Nobl [7] of Vienna obtained excellent results in 90 per cent of 200 cases, but neglected to mention recurrences or the time of observation. Sicard and Paraf,[8] using 10 per cent sodium carbonate in 1917 and 1918, then changing to 20 to 40 per cent sodium salicylate, have treated several thousand patients. No follow-up studies are made available. Bazelis [9] stated that after three years' experience with Sicard's method, no recurrences of veins or ulcers have been observed. Delater [10] laid the blame for recurrences on endocrine disorders, but he failed to state the number of recurrences or the endocrine factors involved. In 500 cases observed over three fourths of a year, Meisen [11] observed no recurrences. Forestier [12] based his results on more than 4,000 injections of sodium salicylate and found 15 per cent recurrences with new varices, not of the old obliterated veins. Sodium chloride in 20 per cent solution gave Goodman [13] from 10 to 15 per cent of recurrences. The time of observation is not stated. Woolsey and Millzner [14] treated over 150 patients with 20 per cent sodium salicylate and with quinine and urethane with 6 per cent recur-

5. Hemple, Curt: Erfahrungen mit Sublimatinjektionen bei Varizen, München. med. Wchnschr. **71**:900, 1924.

6. Fischer, Carl: Ueber Behandlungen der Krampfadern mit Sublimatinjektionen nach Linser und über Behandlung der Beingeschwure, Wien. klin. Wchnschr. **35**:11, 1922.

7. Nobl, G.: Zur künstlichen Thrombose der Varizen, Wien. klin. Wchnschr. **31**:295, 1918.

8. Sicard, J. A., and Paraf, J.: Traitement des varices par l'injection intravariqueuse de carbonate de soude, Bull. et mém. Soc. méd. d. hôp. de Paris **44**: 1369, 1920. Paraf, J., and Lermoyez, J.: Traitement des varices par les injections phlebosclerosantes de salicylate de soude, Gaz. d. hôp. **95**:1573, 1922.

9. Bazelis, M.: Traitement des varices par les injections intravariqueuses, Presse méd. **32**:358, 1924.

10. Delater, G.: Fibrose curative des varices, Presse méd **34**:693, 1926.

11. Meisen, V.: Injection Treatment of Varicose Veins and Their Sequelae on Basis of 500 Treated Cases, Acta chir. Scandinav. **62**:17, 1927.

12. Forestier, J.: Varices of Lower Limbs: Treatment by Obliterating Injections Based on Experience with More Than 4,000 Injections, J. A. M. A. **90**:1932 (June 16) 1928.

13. Goodman, C.: Treatment of Varicosities of Lower Extremities, Internat. Clin. **4**:284, 1928.

14. Woolsey, J. H., and Millzner, R. J.: Varicose Veins: Their Chemical Obliteration, California & West. Med. **30**:325, 1929.

rence in less than fourteen months' time. In sixty-four cases in which 40 per cent sodium salicylate was used, twelve, or 18 per cent, showed recurrences in from three to five months as reported by Cooperman.[15] Kilbourne[16] concluded from the answers to his questionnaire that the recurrence rate is about 6 per cent and quoted Delater as having 5 per cent recurrences after five years. From a communication from Sicard's clinic, he is informed of 1 per cent recurrences at the site of injection and 4 per cent new varices in 15,000 cases. McPheeters,[17] who has published extensively on the subject, failed to mention the percentage of recurrences in his cases, and he is content to state in his monograph that patients are asked to return in from six months to a year, when new varices that have appeared may be readily treated. The most satisfactory study of the treatment of varicose veins by injection that has appeared is the work of De Takats.[18] The last of his series of papers dealing with the subject gives the recurrence rate at 10.8 per cent in 389 cases. He has used the injection method for three years and combines injection with ligation and excision of the saphenous vein in midthigh when it is visibly dilated. De Takats stated that "recurrences were observed as early as six weeks, and as late as a year after injection. While it was impossible to reexamine all discharged patients, they were routinely asked to return every three months. It is probable that a comparatively larger number of patients with failures returned than those cured." Our experience does not bear out this last statement, for those patients who refused to return for observation because they considered themselves cured invariably had recurrences when we examined them at home.

COMMENT

The results of our follow-up examinations with the microscopic studies of the fate of therapeutic thrombosis convince us that treatment by injection unaided by ligature, excision or stripping of main venous channels, and perforating veins when incompetent, will not serve to obtain permanent cure in cases of varicose veins except in the few isolated cases of dilated single veins with competent saphenous and perforating valves. The microscopic studies of veins into which injection has been made have shown the natural history of the thrombus in regard

15. Cooperman, M. B.: Injection Treatment of Varicose Veins, M. J. & Rec. **129**:541, 1929.

16. Kilbourne, N. J.: Treatment of Varicose Veins of the Legs: Considerations of Safety, J. A. M. A. **92**:1320 (April 20) 1929.

17. McPheeters, H. O.: Varicose Veins, Philadelphia, F. A. Davis & Company, 1929.

18. De Takats, Geza; and Quint, Harold: The Injection Treatment of Varicose Veins, Surg. Gynec. Obst. **50**:545, 1930.

to its organization, that is, vascularization and recanalization, a fact so well known to pathologists and so tersely described in the classic article of Welch [19] on thrombosis and embolism as follows:

> One of the most interesting adaptive pathological processes is the so-called organization of thrombi which is the substitution for the thrombus of vascularized connective tissue. The thrombus itself takes no active part in the process, but behaves as a foreign body. It is gradually disintegrated and absorbed, largely through the activity of phagocytes. The new tissue springs from the wall of the vessel or the heart, the tissue forming cells being derived from the endothelium and from other fixed cells in the wall. New vessels spring from the vasa vasorum. Lacunar spaces in the thrombus, or between the thrombus and the vascular wall, may become lined with endothelium, and also serve as channels for the circulating blood. These new vessels may establish communication with the lumen of the thrombosed vessels above or below the thrombus or on both sides. The new tissue which at first is rich in cells, becomes fibrous and contracts. The result may be a solid fibrous plug, or a cavernous structure with large blood spaces; or, by disappearance of the septa, a restoration of the lumen, with perhaps a few fibrosed threads or bands stretching across it, as in the normal cerebral venous sinuses.

The restoration of the lumen is the most frequent end-result in thrombosed veins that are subject to constant back pressure either through the proximal unthrombosed saphenous vein or the perforating veins by their communication with the deep set, when the valves of these veins are incompetent. This principle has caused De Takats to ligate the saphenous vein when it is palpable above the midthigh, in addition to causing thrombosis by injection of the distal veins, and to urge the complete removal of the main saphenous vein with eradication of the perforating branches, when both sets of valves are found incompetent. Several workers, especially Tavel [20] and Moszkowicz,[21] have ligated the saphenous vein at or near the fossa ovalis preliminary to injection, but with the purpose of preventing embolism rather than preventing recurrence, and credit should be given De Takats for formulating the particular plan of ligation and injection for more permanent relief from varicosities.

The most successful treatment of varicose veins by the methods available at the present time is by operation with removal of the saphenous segment from the fossa ovalis to the knee and eradication of the dilated veins below this point at a time when the perforating valves are

19. Welch, W. H.: Thrombosis, in Allbutt, Clifford; and Rolleston, H. D.: A System of Medicine, ed. 2, New York, The Macmillan Company, 1909, vol. 6, p. 701.

20. Tavel, E.: Die künstliche Thrombose der Varicen, Berl. klin. Wchnschr. **44**:181, 1907; Die Behandlung der Varicen durch die künstliche Thrombose, Deutsche Ztschr. f. Chir. **116**:735, 1912.

21. Moszkowicz, L.: Krampfaderbehandlung mit Zuckerinjektionen und Venenligatur, Zentralbl. f. Chir. **54**:1732, 1927.

still competent and ulceration, eczema and edema are yet undeveloped. For permanent results, such a procedure can have no substitute. Far too frequently incomplete measures, such as ligation, ligation with excision of small vein segments or multiple small excisions, are carried out. The experience of the past has shown that these measures are often unsatisfactory. In spite of this the same procedures are carried out because of their relative ease, the patient's fear of extensive operations or their abhorrence of extensive scars and especially because of economic factors that prevent prolonged hospitalization.

SUGGESTED INDICATIONS FOR COMBINED INJECTION AND EXCISION

It is distressing that the majority of sufferers from varicose diseases are small wage earners or overworked housewives whose family resources prevent both hospitalization and means of care for their children while under treatment (an obstacle of some importance). The economic factors will many times determine in the future, as it has in the past, the available method of treatment. It is in this particular situation that the treatment of varicose veins by injection has proved of real value in obtaining relief from suffering and in maintaining ability for productive labor in persons pressed for available time for treatment and lacking financial resources to secure adequate early treatment for permanent relief. With the attitude of adopting the best available method to the particular case under the economic circumstances and using the method of complete operation when possible, we suggest the following indications:

1. When single or isolated dilated vein segments exist in the presence of completely competent valves, symptoms are rarely present. People presenting themselves for treatment of such varices do so mainly for cosmetic reasons. Treatment by injection may be employed entirely.

2. If the patient has moderate dilatation or tortuosity of the saphenous system, provided that the perforating valves are competent, interruption of the venous continuity at the saphenous opening, with injection into the veins below, may be carried out. The interruption of the venous flow may be by ligature with excision of a segment of the vein under local anesthesia, and the treatment may thus be entirely ambulatory. Such a procedure has been successfully carried out by De Takats with promise of lasting results. Tavel utilized this method in 1905, and noticed that in seven of twenty-five cases spontaneous thrombosis occurred distal to the ligature, and apparently permanent cure resulted. Instead of making an injection into the veins distally after an interval of several days following the high excision, as is usually done, one may make the injection into the veins in the wound at the time of operation.

It should be emphasized that ligature and excision should be done at the fossa ovalis, and all tributary vessels emptying into the saphenous vein at this point should be ligated and cut across as well. A double saphenous vein may be present in the thigh, and midthigh ligation of a single vein may fail to give additional benefit. The group of superficial tributary veins emptying into the saphenous vein at the saphenous opening are known to have caused recurrence by opening up of collateral channels following operative excision when these tributary veins were not ligated.

Perhaps a more permanent way of interrupting the back pressure would consist in stripping the saphenous veins from the femoral opening to the knee and making the injection into the veins below this point. The procedure need not necessitate prolonged hospitalization. As De Takats pointed out, the endeavor is to prevent thrombosis and consequent embolism from the deep and proximal veins by early mobilization.

3. When varicose veins are accompanied by incompetency of both saphenous and perforating valves, the complete operation of stripping with excision should be carried out at the expense of temporary loss of time from employment. It is in this type of case that we feel recanalization will occur in spite of complete and repeated thrombosis, and that complete interruption of the continuity of the vein is necessary. Injection into the isolated vein segments may follow such an operation.

4. Those people are poor subjects for operation who have long-standing varicosities with incompetency of both sets of valves and who have extensive chronic ulceration, eczema and a hard, brawny lymph edema approaching the elephantoid condition. The swollen, indurated tissues of the leg hide numerous venous channels and dilated perforating veins which are extremely difficult to eradicate, and in this type of patient the operative results are not brilliant. Such patients are considerably improved but not cured by injection. Injection should be supplemented by the use of sulphurated zinc paste stockings, rest in bed and elevation or skin grafting to hasten healing of ulcers. The edema subsides remarkably but not completely, even under ambulatory treatment, and with the subsidence of the edema the hidden veins become visible or palpable and can be treated by injection. With recurrence of varicose veins, such a patient must receive another injection to hold the improvement gained.

5. Following apparently complete operative excision, varicosities sometimes make their appearance. When this occurs, the new veins are irregular in their distribution and in their connection with the deep set and offer a considerable obstacle to complete reexcision. This type of vein may be properly treated by injection, which will probably have to be repeated.

SUMMARY

In sixty-six patients treated for varicose veins by the injection of 20 per cent sodium chloride, we have been able to reexamine forty-nine a year or more after treatment.

On reexamination, forty-eight of the forty-nine patients showed recurrence of their previously thrombosed veins. Four additional patients were known to have had early recurrence, but could not be located after a year.

The recurrence rate is 79 per cent of all patients treated, or 98 per cent of all those we have followed a year or more.

In contrast, forty-nine had partial or complete relief from symptoms attributed to the varicosities, twenty-eight of these patients being completely relieved from all symptoms.

Recurrence of veins thrombosed by injection was found to take place by recanalization, a natural pathologic response to thrombosis.

The interruption of the continuity of the vein by excision, especially in the presence of incompetent saphenous or perforating valves, is held to be vital in securing more permanent results.

Indications for combining excision with injection are suggested in an effort to afford permanent freedom from recurrence in persons who cannot afford, or reject, the complete excision of varicose veins.

THE FORMATION OF BONE UNDER THE INFLUENCE OF EPITHELIUM OF THE URINARY TRACT *

C. B. HUGGINS, M.D.
CHICAGO

The relative frequency of stones composed chiefly of calcium and phosphorus in the urinary tract as compared with their occurrence in other excretory systems such as the lower intestine, biliary and pancreatic systems and the salivary glands has made a study of the local metabolism of these elements by the urinary tract of some importance. I [1] have indicated elsewhere in a preliminary report the rather unexpected action of the urinary tract on certain connective tissues in the production of bone. These observations will be discussed in detail in this article, and further observations relative to osteogenesis will be presented.

The presence of bone elsewhere than in the skeleton has been of considerable interest to the students of osteogenesis. An extensive literature dealing with this subject exists, of which a few striking examples may be cited. Apparently the most frequent site of heteroplastic bone is the sclerotic artery; [2] next in order possibly comes calcified foci in the lung, and it is not infrequently seen in the dura mater.[3] Not rarely it forms in the eye [4] following severe destructive processes. It has been described in squamous carcinoma of the skin [5] and in carcinoma of the breast, in the fallopian tube,[6] lymph nodes, tonsils and

* Submitted for publication, May 7, 1930.

* From the Department of Surgery, University of Chicago.

* This work was done under a grant from the Douglas Smith Foundation for Medical Research.

1. Huggins, C. B.: Experimental Osteogenesis, Proc. Soc. Exper. Biol. & Med. **27**:349, 1930.

2. Poscharissky, J. F.: Ueber heteroplastische Knochenbildung, Beitr. z. path. Anat. u. z. allg. Path. **38**:135, 1905. Bunting, C. H.: The Formation of True Bone with Cellular (Red) Marrow in the Sclerotic Aorta, J. Exper. Med. **8**:365, 1906. Buerger, L., and Oppenheimer, A.: Bone Formation in Sclerotic Arteries, J. Exper. Med. **10**:354, 1908.

3. Halstead, A. E., and Christopher, F.: Calcification and Ossification of the Meninges, Arch. Surg. **6**:847 (May) 1923.

4. Poscharissky (footnote 2, first reference).

5. Nicholson: Ossification in Calcified Epithelioma, J. Path. & Bact. **21**:387, 1917.

6. Asami, G.: Heteroplastic Bone Formation in the Fallopian Tube, Am. J. M. Sc. **160**:107, 1920.

liver, in fibromyoma of the uterus and in laparotomy scars.[7] It has been stated [8] that any area of calcification is likely to be replaced by bone no matter what tissue is involved.

New formation of bone occasionally occurs in the urinary tract in man or in connection with urologic procedures. Bone was first described in the pedicle attachment of a renal calculus to the pelvis by Phemister,[9] in two cases. It has been described in the abdominal wall following operations on the bladder by Lewis [10] and others.[11] Chauvin and Rouslacroix [12] described five cases of ossification observed by them in three years, subsequent to cystotomy, in the abdominal wall.

BONE FORMATION IN THE URINARY TRACT UNDER EXPERIMENTAL CONDITIONS

Blessig [13] first observed calcification in the kidney of rabbits killed from four to six days after ligation of the left renal artery. Salkovsky (1866) described calcium deposits in the kidney of rabbits poisoned with mercuric chloride; this has been confirmed by many observers.[14] Litten [15] and others [16] have described extensive calcification in the kidney, regularly following temporary arrest of the renal circulation. A demonstrable deposition of calcium [17] may be present as early as thirty-six hours after a temporary anemia of one hour. The calcification occurs in and around necrotic tubules chiefly in two zones, one beneath the cortical surface and the other at the base of the pyramids. Wells [17] stated that calcification produced by temporary anemia as well as by

7. Lewis, D.: Myositis Ossificans, J. A. M. A. **86**:1281 (May 5) 1923. Gruca, A.: Myositis Ossificans Circumscripta, Ann. Surg. **82**:883, 1925.

8. Wells, H. G.: Chemical Pathology, ed. 4, Philadelphia, W. B. Saunders Company, 1920, p. 439.

9. Phemister, D. B.: Ossification in Kidney Stones Attached to the Renal Pelvis, Ann. Surg. **78**:239, 1923.

10. Lewis (footnote 7, first reference).

11. Kretschmer, H. L.: Myositis Ossificans Following Suprapubic Prostatectomy, J. Urol. **20**:477, 1928.

12. Chauvin and Rouslacroix: J. d'urol. **27**:465, 1929.

13. Blessig: Ueber die Veränderungen der Niere nach Unterbindung der Nieren Arterie, Virchows Arch. f. path. Anat. **16**:120, 1859.

14. Weichselbaum: Centralbl. f. allg. Pathol. u. path. Anat. **2**:9, 1891.

15. Litten, M.: Ueber pathologische Verkalkungen und Kalkmetastasen, Virchows Arch. f. path. Anat. **83**:508, 1881.

16. von Werra: Ueber die Folgen des vorübergehenden und dauernden Verschlusses der Nierenarterie, Virchows Arch. f. path. Anat. **88**:197, 1882. Eisendrath, D. N., and Strauss, D. C.: The Effects on the Kidney of Temporary Compression of Its Vessels, J. A. M. A. **55**:2286 (Dec. 31) 1910.

17. Wells, H. G.; Holmes, H. F., and Henry, G. R.: Studies in Calcification and Ossification, J. M. Research **20**:373, 1911.

certain poisons is probably analogous to calcification of organic material in urine rather than calcification of tissues with lime salts direct from the blood, since the epithelium and tube-cast deposits seem to contain calcium only as phosphate with no demonstrable carbonate. When the necrosis and calcification involve interstitial tissues, carbonate can be demonstrated.

An important experiment leading to the formation of bone and bone-marrow in the kidney through permanent ligation of the vascular pedicle was reported by Sacerdotti and Frattin[18] in 1901. These observers described bone occurring in three of four rabbits from seventy-four to eighty-five days after ligation. In two cases the ureter was also included in the ligation. In one experiment at autopsy, some of the pelvis epithelium persisted, and bone formed in spite of the ligation of the ureter; in the other no bone was formed, and the pelvic epithelium had completely disappeared. Poscharissky[4] found bone in three of five animals in which the renal vessels had been tied. Maximow[19] found bone as early as five weeks after ligation of the renal pedicle and described the process in connection with his studies on histiogenesis of blood cells. Liek[20] confirmed the foregoing observations in a series of sixteen rabbits, in four of which he had made a high ligation of the ureters as well as of the vascular pedicle. No bone formed in the latter four. He stated that the necessary requirements for bone formation, namely young connective tissue near calcium deposits, were met following renal pedicle ligation and commented on the relation of the bone to the persisting pelvic epithelium but did not associate the two factors.

This problem has been studied in great detail from a histiogenetic standpoint by Asami and Dock.[21] All observers have noted that bone occurs in thin lamellae in the connective tissue immediately beneath the mucosa of the renal pelvis, and, if of any extent, is exactly parallel to it. It is never found in the scar tissue of the renal cortex, although calcification is constantly present in this location. All authors have stressed the concept of metaplasia of connective tissue into bone through some unknown influence. Asami and Dock concluded "that bone formation in the kidney with ligated pedicle takes place in three ways: (*a*) through

18. Sacerdotti, C., and Frattin, G.: Ueber die heteroplastische Knochenbildung, Arch. f. path. Anat. u. Physiol. **168**:431, 1902.

19. Maximow, A.: Ueber experimentelle Erzeugung von Knochenmarks-Gewebe. Vorlaufige Mittleilung, Anat. Anz. **28**:24, 1906.

20. Liek, E.: Experimenteller Beitrag zur Frage der heteroplastischen Knochenbildung, Arch. f. klin. Chir. **80**:279, 1906; Ein weiterer Beitrag zur heteroplastischen Knochenbildung in Nieren, ibid. **85**:118, 1908.

21. Asami, G., and Dock, W.: Experimental Studies on Heteroplastic Bone Formation, J. Exper. Med. **32**:745, 1920.

the activity of young fibroblasts which accumulate to form a membrane-like structure (resembling periosteum); (*b*) subsequently by direct ossification of hyaline connective tissue in continuity with prepared bone; (*c*) through erosion of lime plaques and laying down of lamellar bone by cells derived from fibroblasts (osteoblasts)."

Pearce [22] observed bone formation following excision of the lower pole (approximately one-half) of the kidney with suture of the defect in six of nineteen kidneys. Bone developed in connection with epithelial buds of the pelvic mucosa. He commented: "For this peculiar localization there is no explanation."

I have observed bone formation beneath the pelvic mucosa in two of three dogs forty days following fulguration of the renal pelvis with an electrical current of high frequency. This was observed once fifty-two days following the application of 95 per cent phenol.

Strauss [23] observed the formation of bone in experimental reconstruction of the ureter in dogs by means of a modified end to end suture of a pedicle flap consisting of the transversalis muscle, fascia and the peritoneum to the ends of the divided ureter. He stated that the peritoneum became replaced by transitional epithelium and the transversalis fascia by bone, and he thought that possibly the tissues became infiltrated with acid from the urine which caused sclerosis and was followed by bone formation.

BONE FORMATION IN THE URINARY BLADDER

Neuhof,[24] in a study of fascia transplantation into vesical defects in eighteen dogs, observed that bone constantly developed in the surface of the fascial patch bordering on the urine and was invariably confined to this fascia. His opinion was that bone formation could be explained only by a metaplasia of connective tissue, and that the genesis of this bone depended on the deposition of lime salts in the necrotive tissue of the fascial patch in contact with the urine. Apparently, he felt that an imbibition of calcium salts took place which stimulated the surrounding connective tissue to build up the most powerful barrier possible, that is, bone. Cartilage was found once in these experiments.

This experiment of Neuhof was repeated, and the observation of bone was confirmed by Phemister [9] who extended his observations to

22. Pearce, R. M.: Notes on the Later Stages of the Repair of Kidney Tissue (Dog) with Special Reference to Proliferation of Pelvic Epithelium and Heteroplastic Bone Formation, J. M. Research **20**:53, 1909.

23. Strauss, A. A.: An Artificial Ureter Made from the Abdominal Wall, Surg. Gynec. Obst. **18**:78, 1914.

24. Neuhof, H.: Fascia Transplantation into Visceral Defects, Surg. Gynec. Obst. **24**:383, 1917.

the rabbit and sheep, which are herbivorous animals with alkaline urine as opposed to the acid urine of the dog. In these animals the fascial patches in vesical defects did not ossify, and he felt that the acid reaction of the dog's urine had something to do with the formation of bone.

Concerning Neuhof's experimental observations, Leriche and Policard [25] commented "In certain places but on the bladder particularly, and constantly the aponeurotic graft gives rise to a plaque of true bone. It is easy to reconstruct the progress of these phenomena. In contact with the calcareous urine, the fascia necroses and is calcified. Around the borders of the old transplant, a proliferating tissue is formed. In proximity to a calcium collection, it ossifies. It is always the same fundamental process. And these experiments undertaken without preconceived ideas are a rigorous demonstration of the mechanism which we have advanced."

Thus it will be seen that certain clinical and experimental observations relative to the formation of bone in connection with the kidney pelvis, ureter and bladder have accumulated. The pathogenesis of this bone was unknown. The following experimental work was undertaken in an endeavor to throw some light on this phase of the subject as well as on the general subject of bone formation.

Axhausen [26] transplanted the gastric and vesical mucosa to the peritoneal cavity in sixteen dogs. The transplants were made to the outside of the stomach or bladder and lasted from fourteen to seventy days. At autopsy he described the formation of cysts lined by epithelium. The fluid in the cysts lined by mucosa of the bladder was dark red, sanguineous in color, as opposed to the light opalescent fluid in gastric cysts. Bone was apparently not observed, for it is not mentioned in this article.

EXPERIMENTAL OSTEOGENESIS

Dogs were used throughout the experiment, except when otherwise indicated. The surgical procedures were carried out under aseptic precautions, ether anesthesia being used. Whenever transplantation of tissue was done, this was autotransplantation. The animals were kept on a varied stock diet. The wounds were sutured with 00 white silk throughout.

EXPERIMENT 1.—This was a critical experiment to ascertain whether the urine played a rôle in the formation of the bone in the fascial transplants to the bladder.

The abdomen was opened; both ureters were isolated and through a stab incision were transplanted to the skin in the groin just above the inguinal ligament.

25. Leriche, R., and Policard, A.: The Normal and Pathological Physiology of Bone; Translated by Moore and Key, St. Louis, C. V. Mosby Company, 1928, p. 194.

26. Axhausen: Die freie Schleimhautüberpflanzung im Experiment, Arch. f. klin. Chir. **102**:121, 1913.

The dome of the bladder was then opened and dried with gauze. A circular piece of fascia 2 cm. in diameter from the anterior sheath of the rectus muscle was then sutured to the edges of the opening in the bladder with a continuous silk suture (fig. 1).

After fifty-five days, the specimen was removed, and along the intravesical portion of the graft a dense button of bone was found strictly confined to the fascial transplant. The transplant was dimpled.

Microscopic examination (fig. 2) showed that the surface of the fascial transplant was covered with the transitional epithelium of the bladder. Beneath the

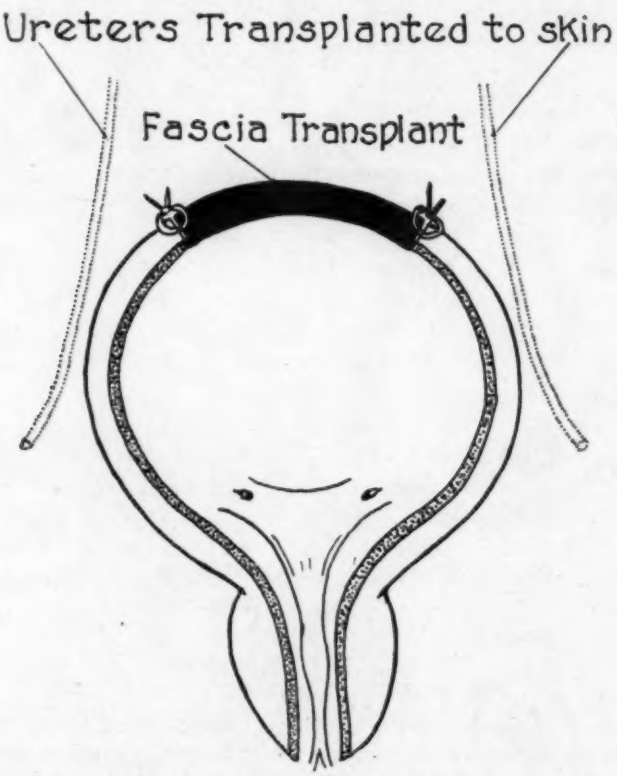


Fig. 1.—Diagram to illustrate experiment 1 in which following bilateral ureterocutaneous anastomosis, fascia was transplanted to the dome of the bladder.

epithelium, but separated from it by a small amount of areolar tissue, there was bone in parallel anastomosing plaques with haversian canals containing bone-marrow, connective tissue and blood vessels. On either side of the transplant at its junction with the wall of the bladder, there had been an ingrowth of epithelial cells in the form of finger-like processes continuous with the epithelial lining of the bladder and the transplant. In the transplant adjacent to these processes, in many places, there were islands of bone (fig. 3), but in the wall of the bladder adjoining this epithelial invasion, there was no bone in any of the sections. This observation is of considerable importance, as will be seen subsequently. The bone

Fig. 2 (dog 337).—Bilateral ureterocutaneous anastomosis, following which fascia was transplanted to bladder. Epithelium covers the transplant, beneath which there is bone formation. An epithelial downgrowth (*A, A*) is shown at the junctions of the musculature of the bladder and fascia transplant. Notice that bone (*B*) occurs only in the transplant. There is no bone on the bladder side of these epithelial processes.

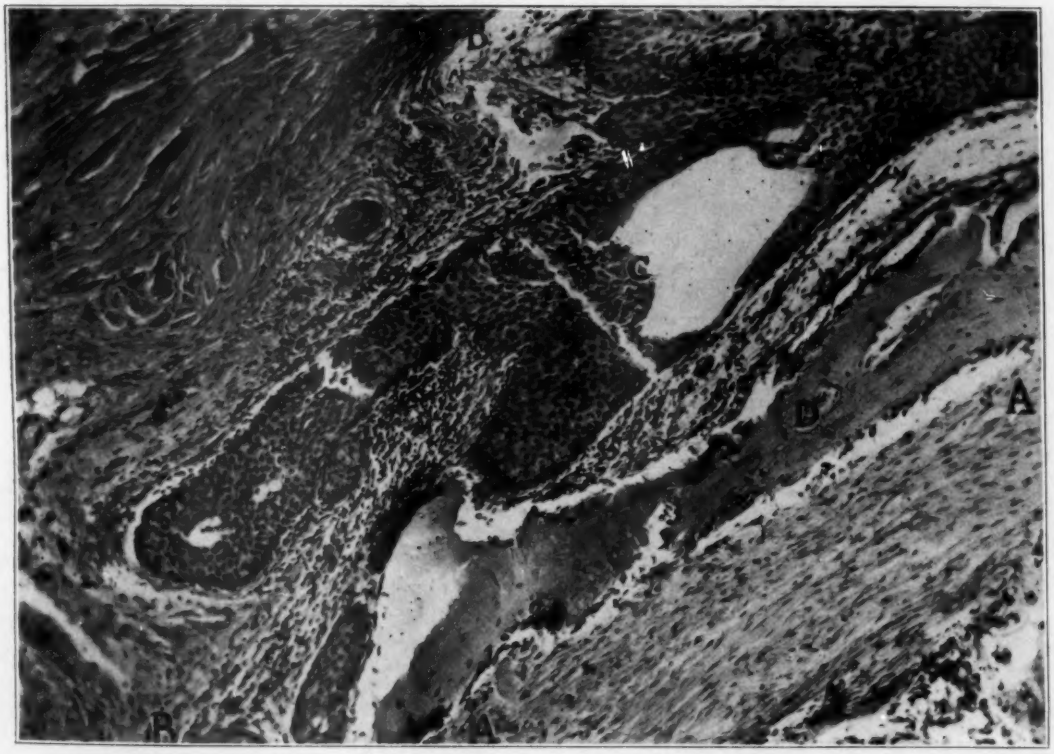


Fig. 3 (dog 337, sixty days, experiment 1).—At the junction of the fascial transplant (*A, A*) and the wall of the bladder (*B, B*), an epithelial downgrowth (*C*) has occurred. Note that the bone (*D*) occurs only in the fascia and not on the bladder wall side of the epithelial process; × 110.

was covered with large numbers of the cells commonly called osteoblasts, indicating an advance in the osteogenetic process. Wherever there was an island of bone, there was an area of vesical epithelium in the immediate vicinity. However, the converse does not hold, for in some of the sections islands of epithelium were seen without accompanying bone.

This experiment was repeated in three dogs, with the same results; it established conclusively that urine is not a factor in the production of bone in this location.

Experiment 2.—Since the urine is not a factor in the osteogenesis in fascial transplants to the urinary bladder, the bone must arise from some anatomic abnormality such as poor circulation or from the influence of some intrinsic element in the wall of the bladder acting on the connective tissue. This experiment was devised to attempt to determine which of these factors was responsible for the osteogenesis.

The abdomen was opened, and a circular area of the muscular coat of the bladder was removed intact by sharp dissection from the smooth glistening mucosa. When this had been done, the shining mucous membrane was moistened with saline, and the remaining filaments of cottony connective tissue were removed as far as possible. All this was done without opening the lumen of the bladder. The mucosa was then incised, and the area of denuded epithelium (2 cm. in diameter) was excised and transplanted on the sheath of the right rectus abdominis muscle, where it was sutured in place with a continuous suture of silk. Similarly, on the sheath of the left rectus muscle the remaining elements of the wall of the bladder, free from epithelium, were sutured in place. The incision in the bladder was then sutured. After sixty days, the first animal was killed.

In the right rectus sheath, a cystic structure was found. The superficial aspect of the cyst was covered with bone, whereas the deep surface was soft, was free from bone, and fluctuation could be demonstrated. The cyst was opened, and 3 cc. of blood-stained fluid was removed. Microscopic examination of the cyst (fig. 4) showed it to be lined by transitional epithelium, histologically not different from that of the bladder. Surrounding one surface of the cyst (that nearest the skin), there was a plate of bone consisting of anastomosing plaques of living bone with fibrous and hemopoietic marrow in the haversian canals. At either end of the cyst (fig. 5) there were finger-like projections of epithelium that were completely surrounded by bone.

In the left rectus sheath, no bone was found, and it was impossible to determine accurately the site of the transplant except by the presence of the silk sutures.

This experiment has been repeated forty-four times with essentially the same results: bone is present in close relationship to the epithelium which has formed a cyst; the bone never completely surrounds the cyst (fig. 4). The presence of epithelium is necessary for the formation of the bone. The bone in all these experiments formed superficial to the cyst. Bone never forms in association with the fibromuscular elements of the wall of the bladder and invariably forms in association with the epithelial transplants, provided the animal lives twenty days or more. In several instances, marked infection of the wound occurred; nevertheless small areas of bone could always be found on careful search. Of course, if the infection were to destroy the entire graft, no bone would form, but this has never been observed. The vesical epithelium is particularly hardy and favorable for transplantation.

Fig. 4.—Camera lucida drawing of a cyst resulting from transplantation of the mucosa of the bladder in rectus sheath illustrating the extent of the bone (fifty-two days). Typical benign papilloma occurred three times in this series as at *A*.

Fig. 5 (dog 74).—Mucosa of bladder transplanted to rectus sheath (sixty-two days). Bone has formed around several islands of mucosa (*A*). The island of mucosa in the lower part of the section is entirely surrounded by bone, whereas the central ring of mucosa is only partly surrounded; × 65.

Fig. 6 (dog 552).—Whole wall of bladder transplanted to rectus sheath (forty-five days). Epithelium, bone and fascia are shown below. The bone is closely adjacent to the newly formed epithelium. Note haversian canals and fibrous marrow; × 38.

EXPERIMENT 3.—A brief outline of the histogenesis of bone derived from bladder transplants in connective tissues is given.

In a series of eight dogs, a circular area of mucosa of the bladder was denuded of its muscular coat and transplanted as in experiment 2. The specimens were excised at various time intervals for microscopic examination.

At seven and nine days, the epithelium was seen to have formed an epithelial lined spheroid containing fluid (fig. 8). The newly formed epithelium was considerably lower than the transplanted epithelium and consisted of a single or double layer of flat or cuboidal cells. At fourteen and sixteen days, the epithelium had formed its more characteristic appearance (fig. 9), and it was difficult to

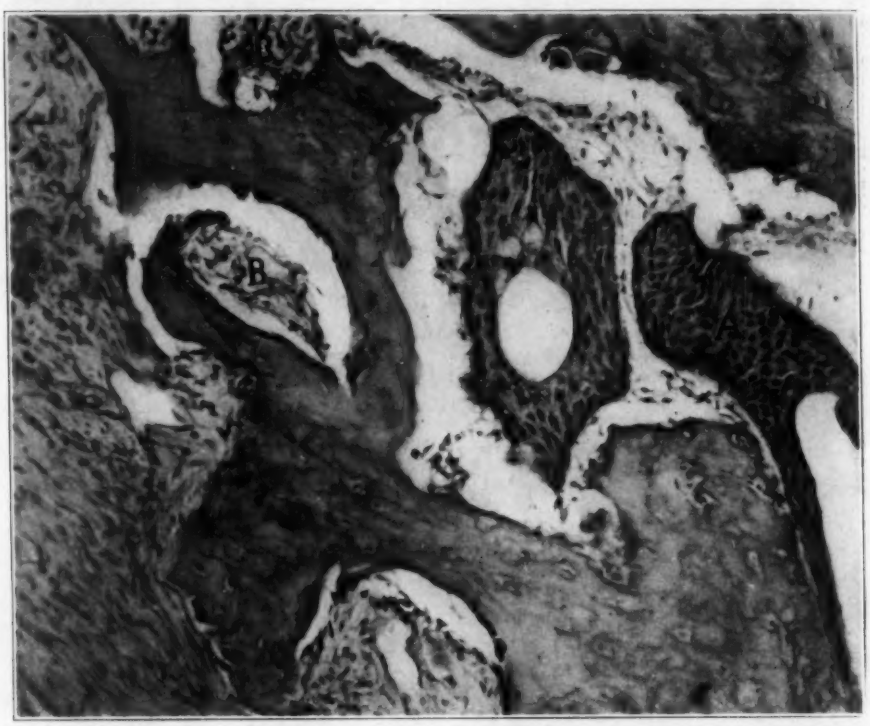


Fig. 7 (dog 74).—Transplant of mucosa of bladder to rectus sheath (sixty-two days). Note relationship of epithelium (*A*) to bone. Haversian canal with hemopoietic marrow at *B*; × 160.

differentiate between the newly formed epithelium and the transplanted mucosa. At this period the connective tissue surrounding a portion of the cyst appeared edematous, and under high magnifications the edema was fibrillary in type. This connective tissue was more eosinophilic and contained fewer nuclei than connective tissue surrounding other portions of the cyst and was presumably a pre-osseous stage in the process.

Nineteen days after the transplant, the first spicules of bone were seen adjacent to the newly formed mucosa. In all transplants older than this, bone was constantly found in connection with the epithelial transplants, and it reached its height about two months after the transplantation.

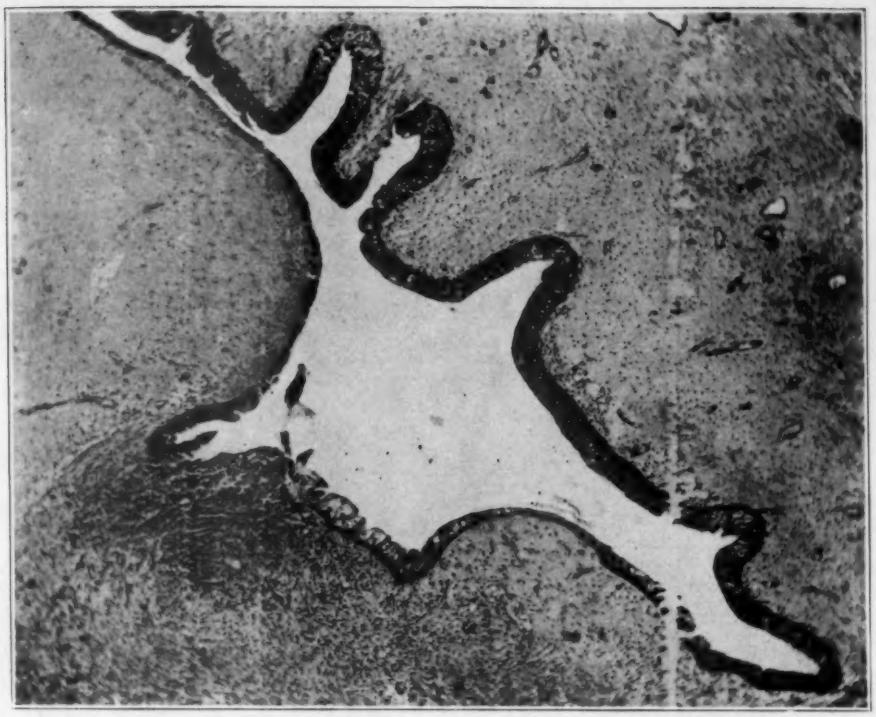


Fig. 8 (dog 595).—Epithelial lined cyst resulting from transplantation of mucosa of bladder to rectus sheath, nine days. The newly formed epithelium is above. Most of the cyst has been included in the photograph; × 43.

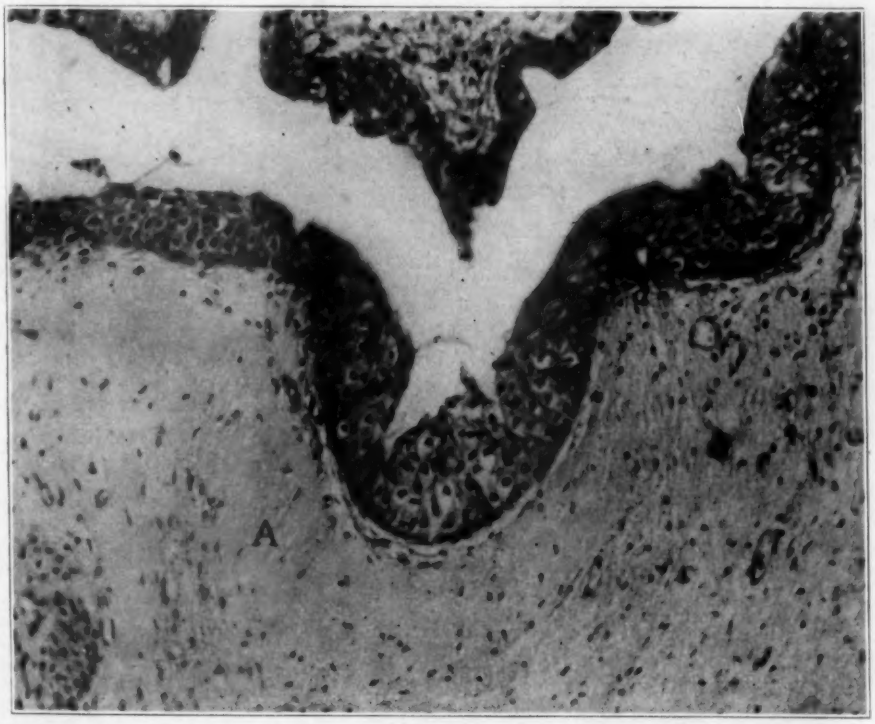


Fig. 9 (dog 689).—Mucosa of bladder transplanted to rectus sheath, sixteen days. The fibrous tissue at *A* is edematous and eosinophilic, and the nuclei are less numerous than in the fibrous tissue elsewhere in the section. Probably preosseous tissue; × 160.

The bone showed little tendency to atrophy and had been observed persisting as late as three hundred and sixty days after the transplant. At this age, however, the bone is not greater in amount than at sixty days.

The bone is typically lamella membranous bone with haversian systems and contains bone-marrow.

EXPERIMENT 4.—Can the location of the bone which forms around a part of the circumference of the cyst developing after a transplant of the mucosa of the bladder to rectus sheath be altered?

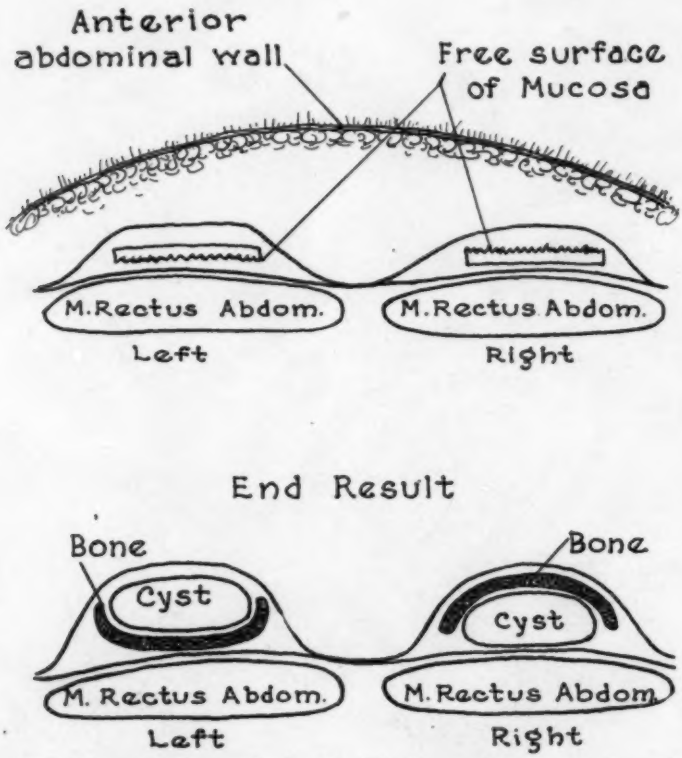


Fig. 10.—Diagram of experiment 4, with the result. Above the wall of the bladder has been transplanted on the left rectus muscle so that the free surface of the epithelium is toward the peritoneal cavity, whereas the mucosa of the bladder on the right, faces in the opposite direction toward the skin. Below, are illustrated the epithelial lined cysts which develop. The bone on the left is situated on the deeper aspect of the cyst, as opposed to the right where it is on its superficial aspect. Bone always forms in the region of the newly formed epithelium.

In this experiment mucosa of the bladder was transplanted to the sheath of the rectus muscle in two equal strips each about 2 cm. in length. A strip was sewed in the right rectus sheath so that its free surface (intravesical portion) faced in the direction of the skin as in experiment 2. On the left rectus, a strip was sewed in so that its deep surface faced the skin, and its free surface faced the peritoneal cavity (fig. 10).

At the end of fifty days, the animal was killed. Each cyst was partly surrounded by bone. The cyst which had formed on the right rectus sheath had bone covering its superficial surface, whereas that which had formed on the left rectus sheath had bone covering its deep surface (that is in the direction of the peritoneal cavity). This experiment was repeated six times, with constant results. The bone formed always in the vicinity of the newly formed epithelium rather than about the transplanted mucosa.

EXPERIMENT 5.—Can cysts lined by mucous membrane from the urinary bladder be developed which will be surrounded entirely by bone?

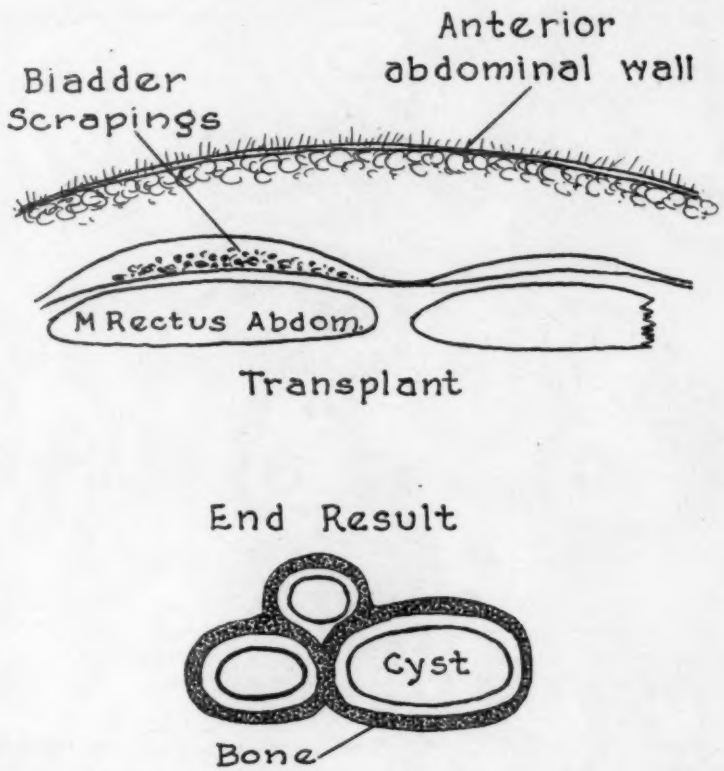


Fig. 11.—Diagram illustrating the deposition of scrapings of epithelium of bladder between the layers of the rectus sheath; below a type of multilocular cyst completely surrounded by bone, which resulted in one experiment at forty-nine days.

In this experiment the urinary bladder was opened through an incision in the vertex; the outer portion of the anterior sheath of the rectus abdominis was then split into its two component layers of fascia for a short distance. The mucous surface of the bladder was then lightly scraped with a sharp knife, and the blood-scrapings thus obtained were deposited in the connective tissue envelop (fig. 11). About one half of the bladder was thus treated, and the hiatus in the rectus sheath was closed by suture. The bladder was then closed.

The dog was killed after forty-nine days; an ovoid multilocular cyst 2 by 2 cm. had formed which was completely surrounded by bone (fig. 12). The cyst was filled with a dark brown serosanguineous fluid.

Microscopic examination showed that the mass was composed of two rather large cysts the bony walls of which were continuous. In the bony walls of these large cysts there were numerous smaller cysts surrounded by bone (fig. 13). All of these cysts were lined by the mucous membrane of the bladder, which in most places was much thinner than that found in the contracted bladder, as if the contained fluid had been under increased tension and had flattened the epithelium. This experiment was repeated four times with similar results, except that the cysts were in no instance as large as in the original experiment. Grossly, however,

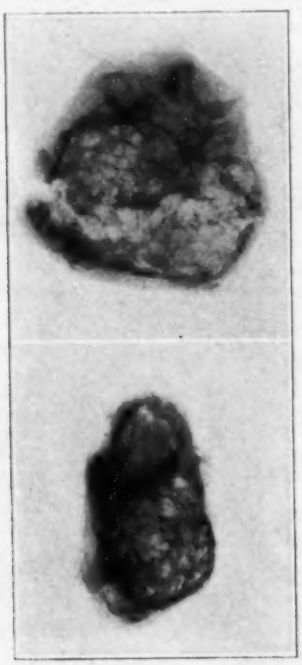


Fig. 12 (dog 47, forty-nine days).—Anteroposterior and lateral roentgenogram of a cyst developed as in figure 11.

the cysts derived from transplantation of scrapings from the bladder were entirely surrounded by bone in every instance, and the bone was in intimate association with the transplanted mucosa.

The factor making for the formation of bone around the entire surface of the cyst seems to be the innumerable small scraping-grafts which must have assumed many different positions, allowing the osteogenetic effect of the proliferating mucosa of the bladder to act in many directions instead of in one as in the previous experiment; in other words, in this experiment there was far greater surface area of proliferating epithelial cells exposed to the fascia.

Experiment 6.—Transplantation of the ureter and kidney pelvis to the parietal fascia will produce epithelial-lined cysts partially surrounded by bone, but similar

transplantation of the cortex or medulla of the kidney or of the prostate does not lead to osteogenesis.

1. The kidney and ureter of a dog were excised, through a median abdominal incision, and pockets were prepared in the fibrous sheath of the rectus abdominis muscle for (*a*) renal cortex, (*b*) renal medulla, (*c*) pelvis epithelium and (*d*) whole ureteral wall. All transplanted tissues were sewed in place by means of silk sutures. The fascia was then closed over these transplants.

After fifty days, the dog was killed and the specimens examined. As has been demonstrated by Didier and Guyon, the renal cortex and medulla did not lead to the formation of bone; the grafts entirely disappeared, and no vestige of them could be found.

The grafts of the renal pelvis and ureter behaved exactly like those from the epithelium of the bladder. Epithelial-lined cysts (figs. 14, 15, 16) formed, surrounded in part by bone; the bone was located in the region of the newly formed

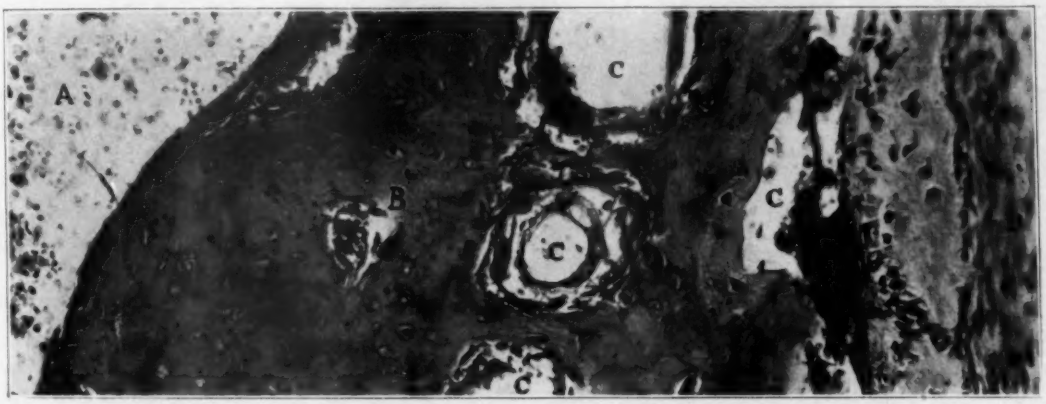


Fig. 13 (dog 47).—Photomicrograph of a portion of a multilocular cyst (fig. 12) entirely surrounded by bone resulting from transplantation of scrapings of bladder into rectus sheath (forty-nine days). *A*, sanguineous fluid in cyst, *B*, bone; *C*, smaller cysts in wall, and *D*, fibrous connective tissue of rectus sheath.

epithelium and was comparable in amount with the vesical grafts of the same age. This experiment was repeated and confirmed in two dogs.

2. In seven dogs the peritoneal cavity was opened through a right rectus incision extending almost to the pubic bone. The bladder was delivered, and the fatty tissue around the prostate was opened by blunt dissection. The prostate was thus exposed and a cuneiform area of prostatic tissue removed, care being taken not to open the urethra. The defect in the prostate was sutured with a continuous silk suture. The prostate graft was then treated in one of several ways: either transplantation in toto by suture to the split rectus sheath, or after morcellation with sand or by a sharp knife, the fragments were deposited in the fascia. The former method gave better results. The transplant was examined ten, fourteen, fifty-four and seventy-two days later. The prostatic tissue usually survived and grew (fig. 17). Bone was not observed associated with prostatic transplants in any case.

Fig. 14 (dog 505-L).—Transplant of mucosa of kidney pelvis to rectus sheath (fifty days). The same relationship of epithelium to bone exists; × 47.

Fig. 15.—Higher magnification (× 130) of figure 11.

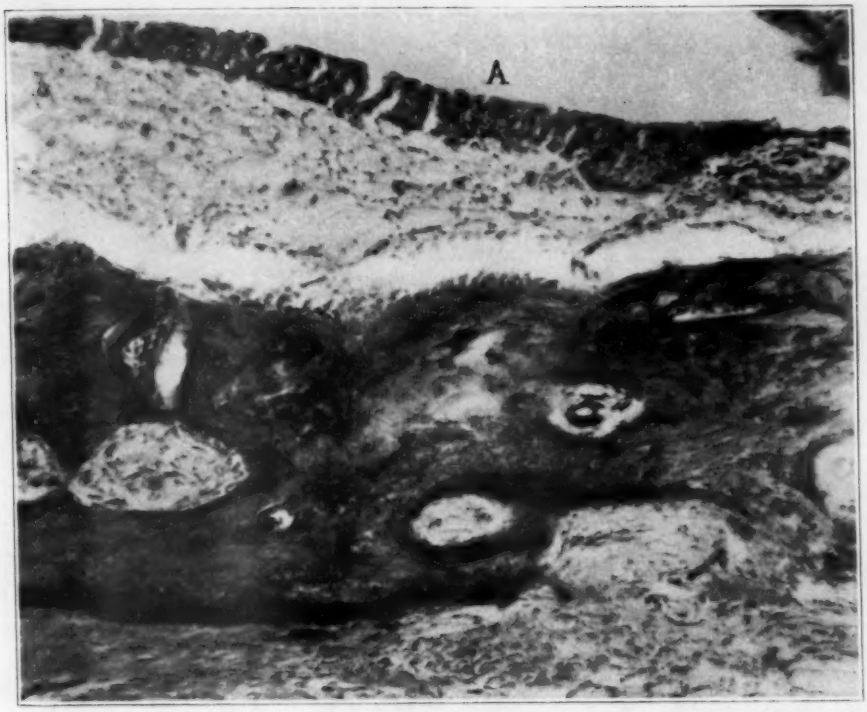


Fig. 16 (dog 505-R).—Transplant of whole ureter wall to rectus sheath (fifty days). Typical membranous bone has formed. Note relation of epithelium (*A*) to bone and that surface of bone is covered with osteoblasts; × 130.

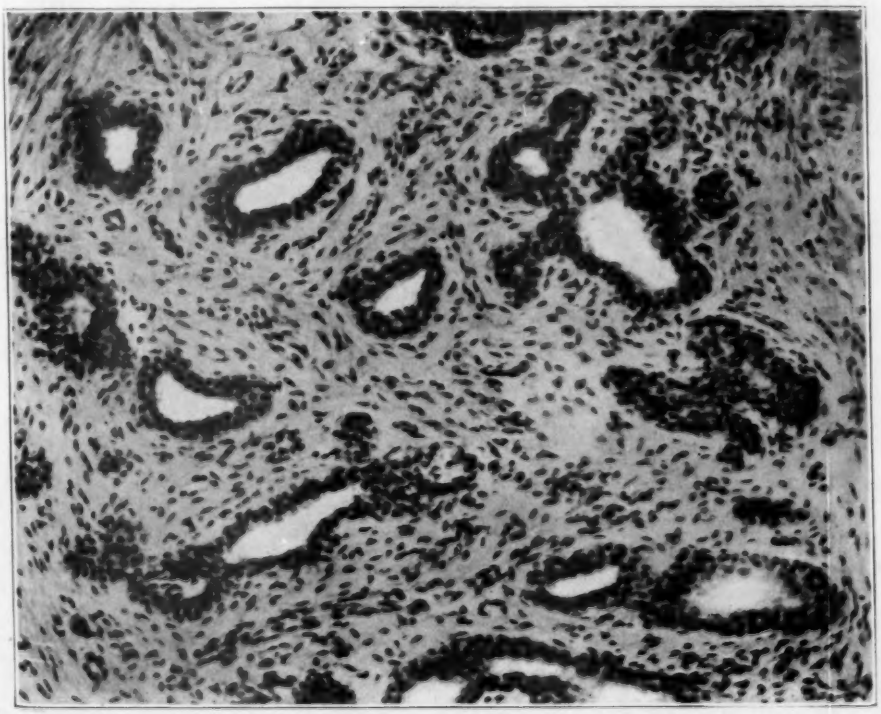


Fig. 17 (dog 691).—Transplant of prostate to rectus sheath, seventy-two days. The epithelium appears normal; there is no bone formation; × 155.

EXPERIMENT 7.—Control experiments: Epithelial transplants were made from the adrenal, gallbladder, stomach, jejunum and colon to the rectus sheath.

The right adrenal gland was removed in three dogs and the cortex was divided into two portions, one of which was transplanted in a puncture wound of the right kidney and the other sewed in the sheath of the rectus abdominis. Section at eighteen, twenty-two and thirty-five days demonstrated the survival of the graft by the presence of yellow tissue, microscopically composed of vacuolated cells arranged in cords. No bone formed (fig. 18).

Free transplants of the gastric mucosa in four dogs (fig. 19), of the wall of the gall bladder in two and of the mucosa of the jejunum and colon in one dog,

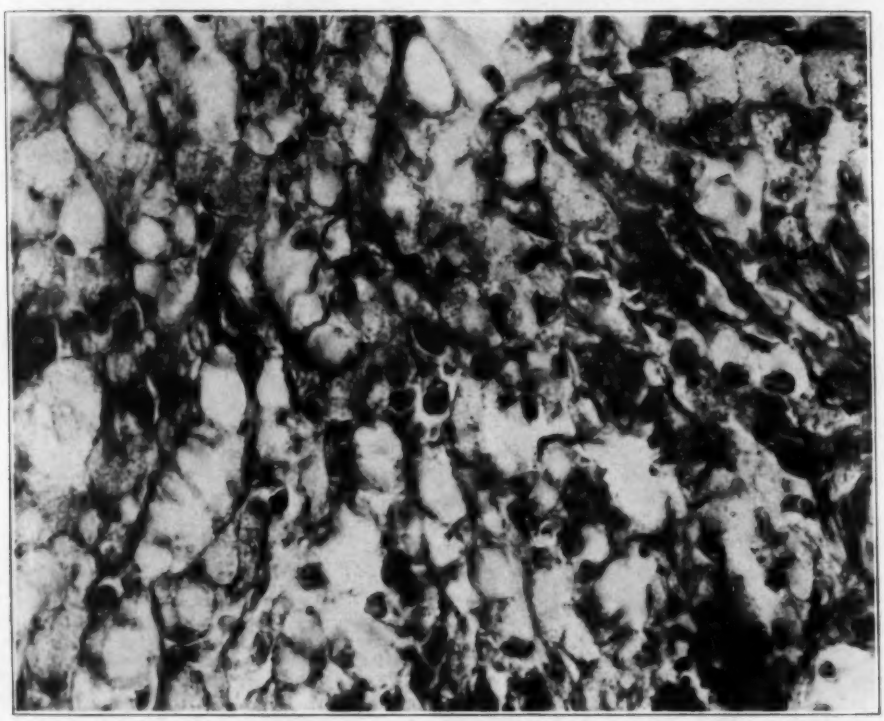


Fig. 18 (dog 132).—Transplant of adrenal cortex to rectus sheath, twenty-two days. The cortex has survived. The cordlike arrangement of lipoid containing vacuolated adrenal tissue is easily seen.

to the abdominal fasciae failed to produce bone in any of the experiments. Small epithelial-lined cysts containing cloudy fluid formed in every instance.

A transplant of the dura mater which was obtained through the elevation of a button of the parietal bone by means of a crown trephine to the rectus sheath failed to cause the development of bone in two cases.

In three instances, thin shavings of bone measuring about 1 by 1 by 0.2 cm. were transplanted to the rectus sheath; these did not lead to osteogenesis. The bone had disappeared in seventy days in two animals, and had diminished greatly in size in the third.

A piece 2 cm. square of the synovia of the knee joint, including the joint capsule, was transplanted to the rectus sheath in two animals; section at sixty days failed to reveal the presence of bone.

The results of the experiments in which bone and periosteum were transplanted as a free graft to fibrous tissue are in accord with the work of Phemister [27] and others, and those of the experimental transplantation of gastric mucosa are somewhat similar to the experiments of Axhausen.[26]

EXPERIMENT 8.—Further evidence indicating the necessity for a proliferating epithelium in the osteogenesis resulting from the influence of the mucosa of the bladder on connective tissue is given.

The abdomen of a dog was opened and the bladder delivered from the wound. With a sharp knife the muscularis and adventitia and peritoneal covering of the

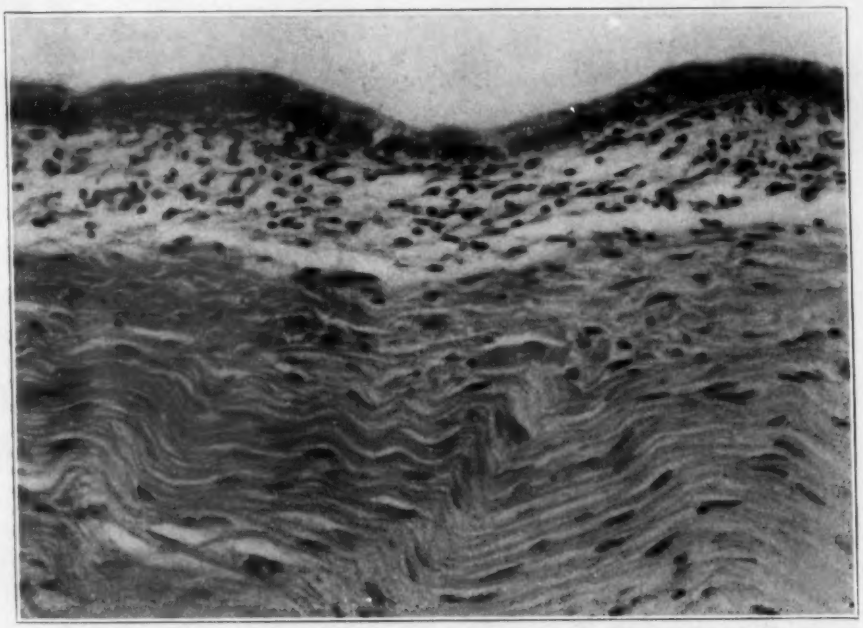


Fig. 19 (dog 81).—Transplantation of gastric mucosa to rectus sheath, seventy-seven days; × 300.

bladder were removed in toto from a circular area of the wall of the bladder 2 cm. in diameter, leaving the shining mucosa of the bladder unopened. A piece of fascia from the rectus sheath was then secured to correspond with the excised portion of the wall of the bladder. This fascia was sutured with silk to the adjacent muscular wall of the bladder to fill the defect (fig. 20). After seventy-six days, the bladder was removed. The transplanted fascia was recognizable by a slightly depressed dimpled area and by the silk sutures. There was no formation of bone in this experiment or in five similar experiments lasting from forty-six to eighty-seven days.

27. Phemister, D. B.: The Fate of Transplanted Bone and Regenerative Power of Its Various Constituents, Surg. Gynec. Obst. **19**:303, 1914; Free Tissue Transplantations, Surg. Gynec. Obst. (Internat. Abstracts Surg.) **18**:333, 1914.

This experimental evidence indicates that a necessary requirement for bone formation is a proliferating epithelium or its products especially since it is known from experiment 4 that bone formed only adjacent to the newly formed epithelium.

Comment.—It seems established by these experiments that proliferating mucosa of the kidney pelvis, ureter and bladder has the power of exciting osteogenesis in the parietal fasciae, and that as far as the tissues described in the group of transplants reported in experiment 7 are concerned, it is a specific effect of the epithelium of the upper urinary tract.

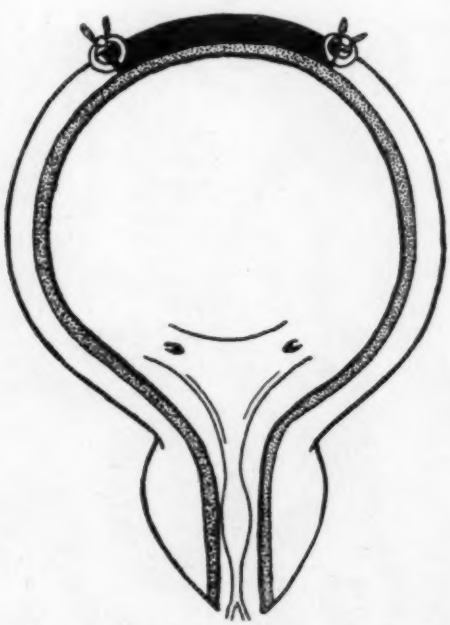


Fig. 20.—Diagram of experiment 8. The fibromuscular elements of a portion of the wall of the bladder have been renewed and replaced by fibrous tissue from the anterior sheath of the rectus. The epithelium has not been opened.

I shall next attempt to establish the fact that there are more factors concerned in this bone formation than proliferating mucosa of the urinary tract and any of the connective tissues and to present evidence that there is a difference between certain connective tissues, so far as they do or do not ossify under the influence of this proliferating epithelium.

EXPERIMENT 9.—The question to be answered by this experiment is whether the combination of proliferating vesical mucous membrane and connective tissue will always produce bone. The experiment is described in two parts.

1. A strip of mucous membrane of the bladder was excised and transplanted (*a*) in the rectus muscle four times, (*b*) on rectus sheath eighteen times, (*c*) in the subcutaneous fatty tissue three times, (*d*) on fascia lata twice and (*e*) on fascia covering the sacrospinalis muscle twice. The animals were killed after a period of from forty-nine to eighty-five days. In each instance, an epithelial-lined cyst developed surrounded in part by bone. The only variation in the results seemed to be quantitative; that is, when the transplant was made between fascial layers or in muscle tissue, more bone formed than when the transplant was made between fat and fibrous tissue or wholly within fatty tissue. This might be

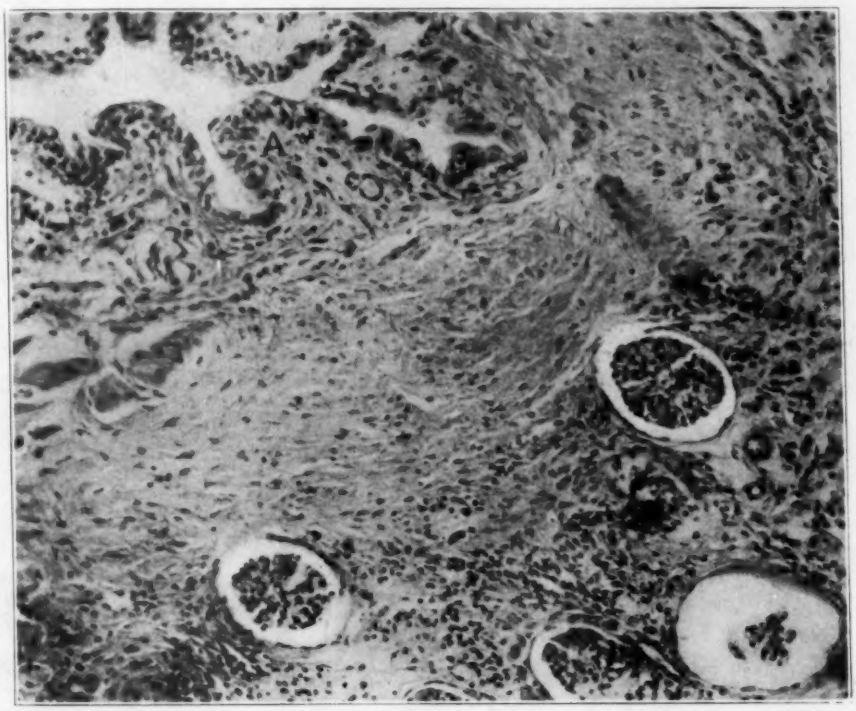


Fig. 21 (dog 434).—Transplantation of mucosa of bladder to the kidney (cortex). A portion of the cyst lined by transitional epithelium which forms is shown at *A*. No bone results; × 130.

expected to have occurred, since there is less connective tissue in the subcutaneous fatty deposits than in the muscle or muscle sheaths.

A similar strip was inserted in the synovial cavity of the knee joint in three dogs and allowed to remain from forty-one to fifty days; the wound was closed in layers and a plaster cast was applied for ten days. The mucosa became attached to the synovial membrane forming a plaque of bone, near the patella, in two cases laterally and in the third medial to that sesamoid. At the conclusion of the experiment, a slight increase of synovial fluid was found. In no case were there loose bodies.

2. A strip of mucous membrane was excised from the bladder and placed in the parenchyma of (*a*) the kidney, (*b*) the liver, (*c*) the spleen and (*d*) the lung. Each experiment was done in three dogs.

The animals were killed from thirty-five to ninety-six days after the transplant was made. In no instance did bone develop.

In the lung, the transplant invariably became infected, and a chronic abscess of the lung was found at autopsy.

In the kidney, liver and spleen (figs. 21, 22, 23) well formed epithelial lined cysts were found. Microscopic examination showed that the cysts were lined by transitional epithelium and had been surrounded by connective tissue. From his-

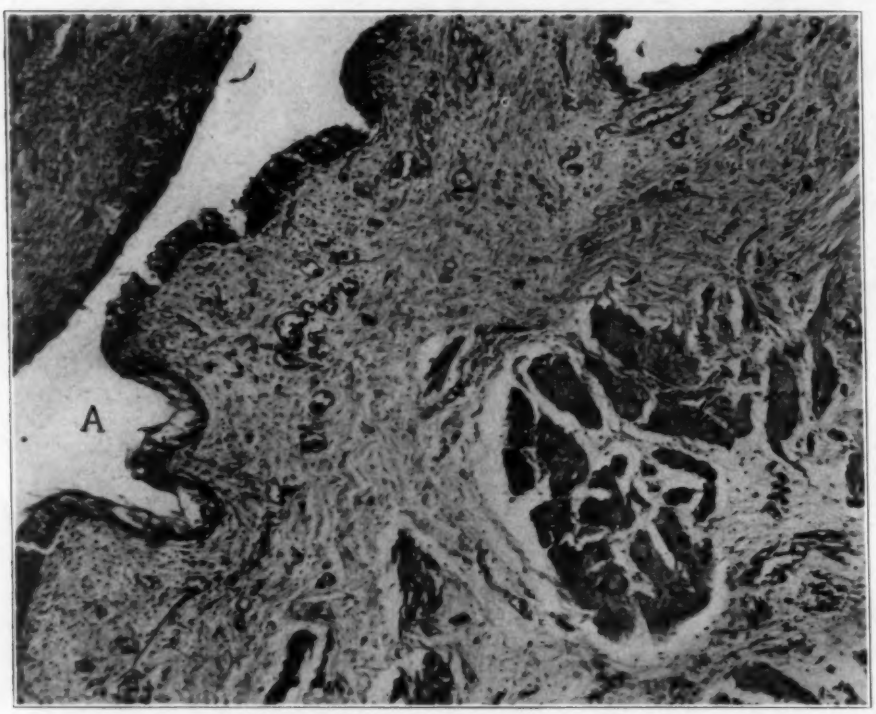


Fig. 22 (dog 929).—Transplantation of mucosa of bladder to liver. An epithelial lined cyst (*A*) surrounded by connective tissue forms but no bone; × 90.

tologic evidence, it was impossible to see any difference in either the epithelium or the connective tissue, and in cysts of the same age in the sheath of the rectus. Here obviously the difference between bone formation in these parietal connective tissues and its absence in the organs mentioned must lie in a chemical or physical difference in the connective tissues, since the epithelium and the morphologic appearance of the fibroblasts are the same.

EXPERIMENT 10.—Since it has been reported that transplants of connective tissue to the dome of the bladder in the rabbit will not ossify (Phemister [9]), the question arose whether free transplants of mucosa of the bladder into fascia will form bone in this animal.

In six rabbits the urinary bladder was opened and the dome excised; the bladder was then closed by a continuous Lembert suture, followed by a purse-string suture which held in place the inverted dome of the bladder. The excised dome of the bladder was then sewed in the sheath of the rectus abdominis muscle with silk. In two of the animals infection followed operation, and here a tumor the size of a hen's egg was palpable beneath the skin. One of these animals was killed at the end of thirty days and the other after a hundred and forty-five days. Necropsy showed the tumor to be composed of a dense mass of yellow caseous tissue, thoroughly inspissated, from which bacteriologic examination showed *B. subtilis* in almost pure culture. In the animal killed after one hundred and forty-

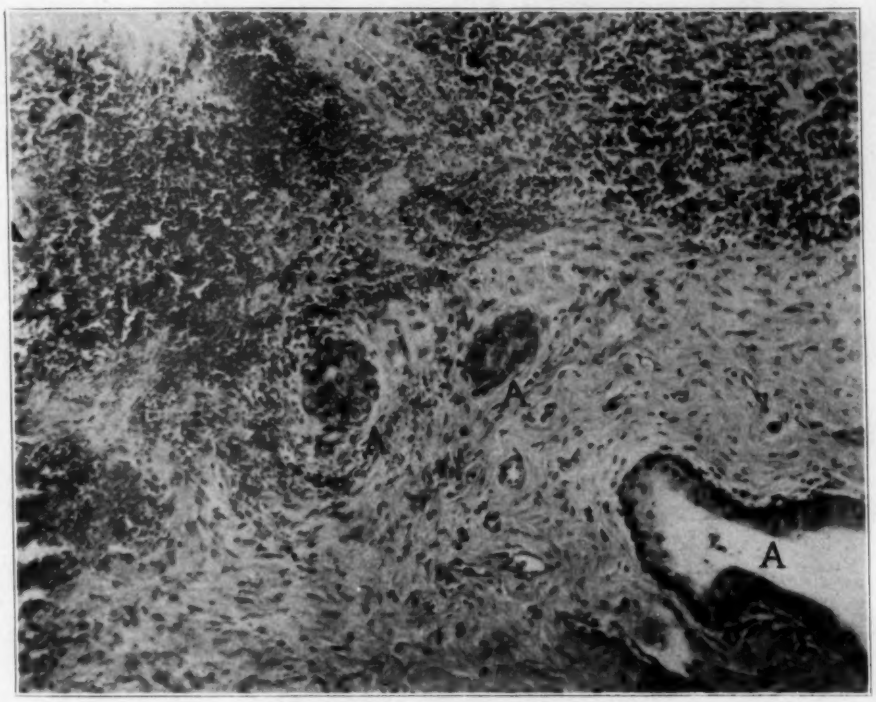


Fig. 23 (dog 10).—Bladder epithelial transplant to spleen. The epithelium (*A, A*) is surrounded by connective tissue, but no bone has formed; × 55.

five days, the wall was calcified. There was no evidence of the mucosa of the bladder in either experiment. The tumors were chronic pyogenic abscesses. The remaining four animals were killed after sixty, seventy-one, eighty-four and ninety-five days. All the experiments were negative for bone except that lasting ninety-five days. In each a cyst was found lined by epithelium of the bladder containing fluid and surrounded by connective tissue. In the animal killed after ninety-five days, a plaque of bone 1 cm. in diameter was found adjacent to the vesical mucosa in the rectus sheath resembling the observations on the dog.

EXPERIMENT 11.—Since the mucosa of the bladder of the rabbit forms bone only under exceptional circumstances when transplanted to the rectus fascia, is the failure of bone deposition a local or a general process? Experiment 10 was

repeated with the addition of the administration of large doses of viosterol or of parathormone.

Seven rabbits were operated on as in the last experiment. From three to six days later, viosterol in oil 1,000 D, was given to the rabbits in doses of 2 cc. daily by stomach tube. This was given every second day.

One rabbit died after three doses and one after five doses. The remaining rabbits were given between eight and fifteen doses. Necropsy after from thirty-five to forty-nine days revealed the usual observations of massive doses of viosterol in rabbits, such as a marked deposition of calcium in the aorta and somewhat less in the kidney and other organs. The usual epithelial-lined cysts were found, but bone was not present. It is interesting that necropsies of the animals four and five months after the feedings with viosterol were stopped showed virtually no regression in the calcification in the aorta.

Two rabbits were similarly treated, except that six units of parathormone given subcutaneously every second day was substituted for the viosterol over a period of thirty days. Three rabbits were similarly treated, except that eight units of parathormone was administered every second day for ninety-eight days.

Autopsy of the five rabbits showed well formed cysts lined by mucosa of the bladder and containing the usual sanguineous fluid in four; in the fifth no trace of the transplant could be found (infection?). No bone was found in any of the experiments. Thus the agents that will cause the deposition of bone in man or rickets produced experimentally or that will normally raise the blood calcium did not induce ossification; this is interpreted as evidence that in the rabbit the failure of the epithelium to stimulate bone formation in the rectus sheath is due to local conditions in either the epithelium or the rectus sheath rather than to general causes such as a lack of vitamin D or hypocalcemia.

It is known from the earlier observations in the literature [28] that under certain conditions bone forms in the urinary tract of rabbits (and my work would suggest strongly that it is due to the action of the proliferating pelvic mucosa) as well as in the single instance cited in experiment 10. Therefore it would seem as if the rectus fascia of the rabbit were lacking in the attributes necessary for bone formation when epithelium of the urinary tract is transplanted to it.

Experiment 12.—If the epithelium of the bladder influences at times the laying down of bone in certain connective tissues, why is bone a rare observation in the bladder itself where proliferating, epithelial processes are common as a result of infection, stone, operations, etc.?

In three dogs, the bladder was opened through an incision in the vertex. With a knife, the mucosa of the bladder was dissected from the parietal tissues. This is technically an easy procedure. The musculature of the bladder was thus denuded of epithelium except for a triangular area in the trigone and an irregular ring around the urethrovesical junction. Hemostasis was secured by the aid of a hot gauze pack inserted in the bladder and pressure from without on the pack. After hemostasis was complete, the incision in the dome of the bladder was sewed with two rows of silk, with care not to encroach on the denuded muscularis more than was necessary. In one of the animals it was found that a sheet of mucosa 8 by 5 cm. had been thus removed and in the others relatively large areas. These animals were killed after eighteen, thirty-five and forty-one days.

It was interesting to observe that the musculature of the bladder denuded in this manner was competent to prevent leakage into the peritoneal cavity. At thirty-five and forty-one days it was found that the epithelium (figs. 24 and 25)

28. Poscharissky (footnote 2, first reference). Sacerdotti and Frattin (footnote 18). Maximow (footnote 19).

had completely regenerated, lining the bladder. The wall was considerably thicker than normal, and distention was limited. The macroscopic and microscopic studies will be presented elsewhere. It is sufficient to state here that bone did not form in the wall of the bladder which is probably in a similar class with the other tissues that do not ossify under the influence of proliferating mucosa of the bladder.

Comment.—It will be seen that there are apparently two classes of fibrocytes which react differently to the presence of adjacent proliferat-

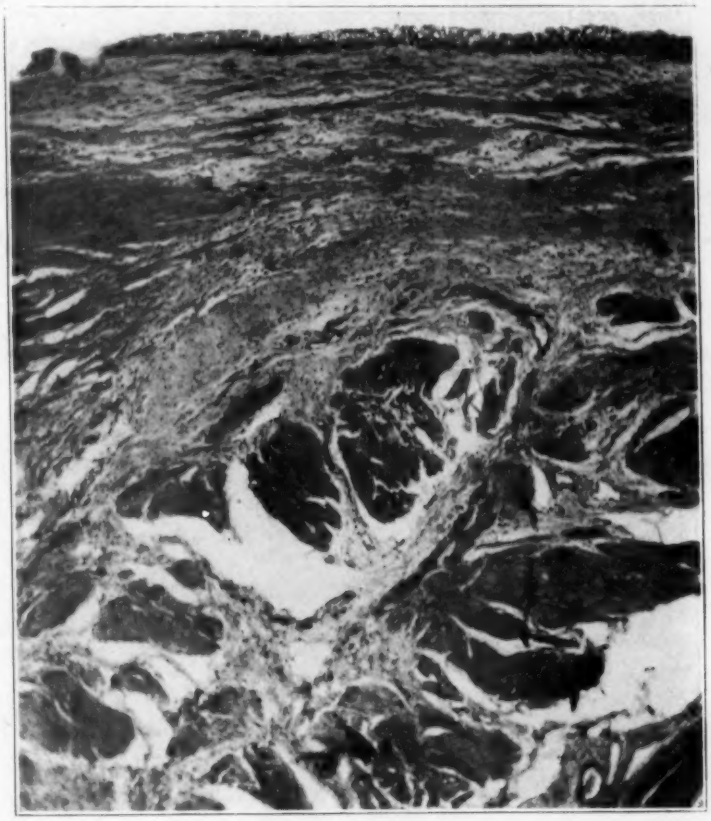


Fig. 24 (dog 546).—The mucosa was cleanly removed from the bladder except a small strip at the base, and bladder incision closed. The regeneration of the transitional epithelium is shown (forty-one days). An hypertrophied fibrous tela submucosa has formed limiting distention of the bladder. No bone formation; × 55.

ing epithelium of the bladder, one which is susceptible of being ossified and the other which is not. In the first class (ossifying), are the connective tissues of the fatty-fibrous subcutaneous tissue, of striated muscle, of the fasciae (rectus sheath, fascia lata, fascia covering

sacrospinalis muscle) and capsule of the knee joint in the dog and the fibrous tissue that forms beneath the proliferating pelvic epithelium after ligation of the renal vessels in the rabbit.

In the second class (nonossifying) are the fibromuscular wall of the urinary bladder and connective tissue stroma surrounding transplants of mucosa of the bladder in the liver, spleen and kidney in the dog and the fascia of the rectus sheath and the fascia lata in the rabbit.

The physiologic difference between these fibroblasts which under the microscope seem identical is not apparent, but it seems clear that such a difference exists.

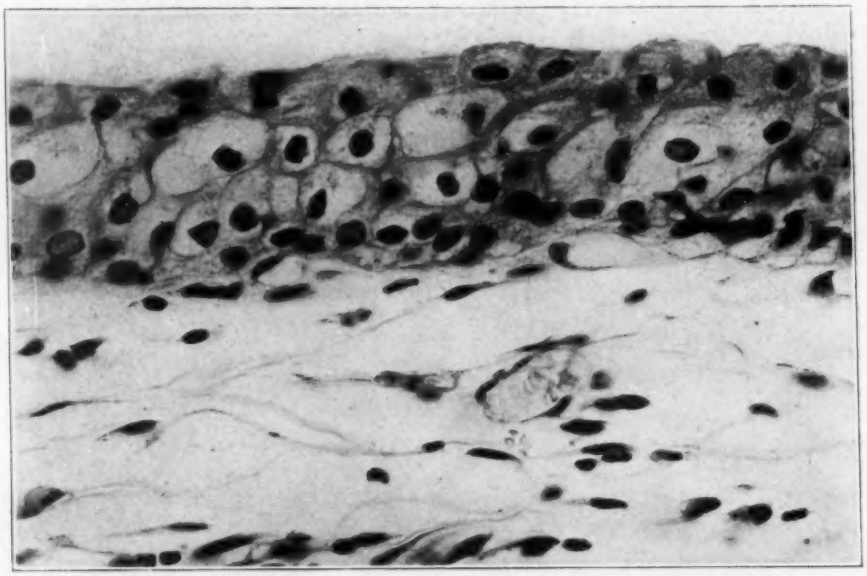


Fig. 25 (dog 546).—Higher magnification of regenerated epithelium shown in figure 21; × 560.

EXPERIMENT 13.—Will fascia introduced into the fluid contained in cystic epithelial transplants of bladder to rectus sheath, in part surrounded by bone, ossify?

The result of this experiment are incomplete. Five experiments have been conducted as follows: A circular area of mucosa of the bladder 2 cm. in diameter was excised and transplanted between the internal and external oblique muscles; after bone had formed as determined by palpation through the skin, a second incision was made exposing the cyst, which was entered through a small incision in its surface that was not surrounded by bone. A small piece of fascia was then excised from the rectus sheath and inserted in the lumen of the cyst, the wall of which was then closed by a silk suture.

In dog 212, the original transplant to the rectus sheath was made on Oct. 30, 1928. An easily palpable plaque of bone about 3 cm. in diameter formed around the cyst. A small piece of fascia was inserted in the cyst two hundred and ninety-

eight days later. Examination forty-seven days after this second operation showed an irregularly spherical mass of bone about 4 mm. in diameter lying free in the cyst fluid. Gross examination showed that the mass consisted of a shell of bone completely surrounding a core of fibrous tissue. Microscopic examination demonstrated the fibrous tissue core as living and surrounded by true bone. The bone, however, was lamellar with haversian system. The microscopic appearance of the bone (fig. 26) is thus different from areas of bone known to be growing in "tissue

Fig. 26 (dog 212).—Roentgenogram and photomicrograph of bone which formed around a piece of connective tissue inserted in the fluid of an epithelial cyst caused by the transplant to mucosa of bladder and rectus sheath. Judging from the cancellous spaces, the fibrous tissue had become attached to the epithelial wall, although at autopsy the bone was found free as a loose body.

culture," such as the osteocartilaginous loose bodies sometimes observed lying free in joints in man, which are known to be growing free in the synovial fluid However, the presence of the loose body of bone with a central core of fibrous tissue would strongly suggest that the introduction of the fibrous tissue played a part in the formation of this shell of bone; it probably became attached to the wall in some way, later coming loose after bone had formed.

In two other animals, at necropsy thirty-one and thirty-seven days after the introduction of fascia, the fascia was found intact but not viable and not surrounded by bone. In two animals at necropsy forty-one and ninety-three days after this procedure, no fascia was found.

EXPERIMENT 14.—Will the introduction of a silk suture in the lumen of an epithelial-lined cyst of the mucosa of the bladder lead to the deposition of salts on it as frequently occurs around nonabsorbable sutures in the lumen of the bladder?

The presence of stone around a silk or linen suture in the bladder is an extremely common experimental and clinical observation. It was with some interest, therefore, that a piece of sterile silk 3 cm. in length was introduced as a loose body into the fluid secreted by the vesical epithelium in these cysts partly surrounded by bone. It was done three times, and the experiment was allowed to run thirty, thirty-seven and forty-seven days.

Examination in the thirty and forty-seven day experiments showed that a part of the thread had become surrounded by bone in the wall of the cyst to which it was attached. In the thirty-seven day experiment the entire thread was found lying free in the lumen of the cyst, as a part had been in the first two animals. In no case had gross precipitation of calcium salts occurred on the threads.

EXPERIMENT 15.—This experiment was a study of the fluid in epithelial-lined cysts resulting from transplantation of the mucosa of the bladder to the sheath of the rectus abdominis muscle, especially of the calcium and phosphorus content. (The chemical determinations were made by Dr. E. L. Compere.)

When a circular area of the wall of the bladder 2 cm. in diameter is transplanted to the rectus sheath, a cyst forms containing a dark brown, sanguineous fluid, which does not clot spontaneously in three hours. Microscopic examination shows it to be made up chiefly of erythrocytes in various stages of degeneration, with a few leukocytes and desquamated epithelial cells. The amount of the fluid is rarely more than 4 cc., usually about 2 cc.

It seemed of interest to determine the calcium and inorganic phosphate content of this fluid and to compare the results with similar simultaneous determinations on the blood serum. In addition, in some experiments the hydrogen ion concentration and the carbon dioxide content of the fluids were determined.

The fluid was aspirated through the skin with an 18 gage needle and drawn under oil. Calcium was determined by the Collip [29] modification of the Kramer and Tisdall [30] method in most instances. In three of the determinations, the organic material was destroyed by heating with concentrated sulphuric acid before using the foregoing method, with approximately the same results. Inorganic phosphates were determined by the method of Fiske and Subbarow.[31] The carbon dioxide content of the serum and cyst fluid was determined by the manometric method of Van Slyke and Neill.[32] The bicolormetric method introduced by Myers [33] and Hastings [34] was used for the hydrogen ion concentration.

---

29. Clarke and Collip: J. Biol. Chem. **63**:461, 1925.

30. Kramer and Tisdall: J. Biol. Chem. **47**:475, 1921.

31. Fiske and Subbarow: J. Biol. Chem. **66**:375, 1925.

32. Van Slyke and Neill: J. Biol. Chem. **61**:523, 1924.

33. Myers: J. Biol. Chem. **54**:675, 1922. Myers, Schnitz and Booher: J. Biol. Chem. **57**:209, 1923.

34. Hastings and Sendroy: J. Biol. Chem. **61**:695, 1924.

The results are tabulated in table 1. In ten of thirteen determinations, the calcium was decidedly elevated above the blood serum calcium. In five of eight determinations, the inorganic phosphate content of the cyst fluid was markedly increased over the values for blood serum. In eight of nine determinations, the cyst fluid was more acid than the

TABLE 1.—*Hydrogen Ion Concentration, Calcium and Phosphorus Content of the Fluid Found in Epithelial Lined Cysts of the Bladder Mucosa (Experiment 15) as Compared with Similar Values of Blood Serum in the Dog*

			Cyst Fluid					Blood Serum				
Dog No.	Date	Days Transp.	Cc. of Fluid	Ca*	P*	CO_2†	p_H	Ca*	P*	CO_2†	p_H	Ossification in Cyst
256	9/10/29	62	3.0	15.9	11.0	....	6.32	10.4	5.16	43.16	7.51	++++
212	9/10/29	47	3.6	15.6	9.6	....	6.45	10.98	3.44	49.2	7.57	++++
215	9/14/29	80	5.4	10.77	8.23	....	6.35	10.77	4.91	....	7.43	++++
543	11/18/29	29	2.6	13.35	....	....	7.35	10.34	....	....	7.42	++++
543	12/18/29	59	10.0	10.72	5.9	....	6.97	11.07	5.33	....	7.53	Cyst fluid contains pus
689	2/ 3/30	33	2.2	.....	....	16.4	7.27	11.6	5.3	45.3	7.44	++++
724	2/ 3/30	57	5.0	.....	....	18.3	7.02	10.8	5.71	51.5	7.45	++++
986	2/ 3/30	35	9.0	11.04	4.4	28.6	7.17	11.2	5.16	51.3	7.44	++
821	3/10/30	62	0.5	16.3	....	....	....	11.6	6.15	....	....	++++
986	3/10/30	69	0.8	15.2	....	....	....	11.6	6.2	....	....	++++
928	2/ 3/30	100	6.0	.....	....	114.7	7.69	12.20	6.66	55.9	6.92	+ Cyst grossly infected
873} 506}	3/10/30	49} 62}	0.65	17.4	....	....	....	11.86	6.25	....	....	++++
212	6/24/29	267	3.0	23.5	....	....	....	10.5	....	....	....	++++
821	4/16/30	113	1.5	18.2	5.22	....	....	12.6	6.67	....	....	++++
689	4/16/30	118	1.8	16.6	3.0	....	....	12.6	6.67	....	....	++++
869	4/11/30	67	2.4	16.0	16.8	....	....	10.46	6.4	....	....	++++

* Milligrams for each 100 cc.
† Carbon dioxide content per cent by volume.

TABLE 2.—*Hydrogen Ion Concentration and Phosphorus Content of the Blood Found in Cysts of the Bladder Mucosa in the Rabbit, as Compared with Blood Serum (Experiment 15)*

			Cyst Fluid					Blood Serum				
Rabbit No.	Date	Days Transp.	Cc. of Fluid	Ca*	P*	CO_2†	p_H	Ca*	P*	CO_2†	p_H	Ossification in Cyst
348	12/30/29	50	0.75	.....	7.16	....	7.32	.....	7.02	....	7.35	No ossification
353	12/30/29	50	0.6	.....	7.4	....	7.34	.....	6.7	....	7.39	No ossification
362	12/30/29	50	1.0	.....	6.7	....	7.35	.....	7.04	....	7.34	No ossification

* Milligrams for each 100 cc.
† Carbon dioxide content per cent by volume.

blood serum. The carbon dioxide content of the cyst fluid was much less in three of four determinations than the normal values obtained at the same time from the blood serum.

In three rabbits the phosphorus content and the hydrogen ion concentration of the blood serum and of the fluid of the bladder cyst were determined. Table 2 shows the results in tabular form. The phosphorus content and p_H did not vary strikingly from the values for blood serum.

In all of these determinations it must be realized that small amounts of fluid were necessarily used, so that the possibility of error is greater than if larger amounts could have been obtained. In three transplants in dogs, large amounts of fluid were obtained; these cases were probably not true cysts lined by transitional epithelium, but abscesses, since gross pus was seen. However, in each of the abscesses bone was found, but in two cases it was small in amount; this showed that the graft had apparently survived, at least in part. Ruling out these cases of gross infection, it will be seen that in the remaining cases the calcium content of the cyst fluid was markedly elevated above the value for serum calcium.

COMMENT

The proliferating mucosa of the kidney, ureter and bladder is a sufficiently strong stimulus to certain connective tissues in the dog and rabbit to induce the formation of bone. Certain other fibrocytes do not react in this way. The exact physicochemical change thus affecting the fibrocyte is unknown, as well as the mechanism of resistance to bone formation on the part of tissues in which bone does not form.

It seems logical, since the cyst fluid in most cases contained much more calcium and phosphorus than did the blood serum, to assume that this has a bearing on the problem, especially since in certain cases, as in experiment 1, a cyst did not form, and the fluid secreted by the cells must have been disposed of in the tissues themselves. It must be granted as proved that the mucosa of the bladder in this position secreted [35] calcium and phosphorus into the lumen of the cyst.

It is possible that the newly formed epithelium, lining the cysts which form when mucosa of the urinary tract is transplanted to the rectus sheath in the dog, is more permeable to the fluid secreted by the epithelium than the older mucosa. This would explain the occurrence of the bone in the vicinity of the proliferating epithelium.

Since this osteogenesis occurs invariably (barring severe infection), this method affords a way of studying osteogenesis that offers certain advantages over that of osteogenesis from preexisting bone, periosteum or cartilage. The exact duration of the osteogenic stimulus is known in this experiment. Moreover, a fluid is present which may aid in the study of osteogenesis.

The production of bone under the direct influence of epithelial cells is proved for the first time by the experimental method. The observation of epithelial cells infiltrating bone is common in certain osteoplastic processes in the skeleton resulting from tumor invasion. This is frequently seen in man in the metastases of prostatic carcinoma to bone,

35. Further unpublished studies by F. H. Entz in this laboratory indicate that the mucosa of the bladder normally secretes calcium and phosphorus.

and is seen in the hyperostosis overlying cranial meningiomas,[36] as well as in other tumors.

Two views have been expressed regarding the pathogenesis of the bone in tumor metastasis. Von Recklinghausen and others explained this process as due to a stimulation of new bone by passive hyperemia due to venous obstruction by tumor cells. The second view has been advocated by Axhausen and others who believe that the new bone forms as a result of stimulation of the surrounding osteogenic elements by chemical substances formed by the tumor cells.

These experiments, which demonstrate a direct relationship between osteogenesis and certain epithelia, favor the second hypothesis, especially for metastases of carcinoma from the prostate, because of the ontogenetic relationship of the prostate to the urinary tract. Osteogenesis, however, has not occurred about prostatic transplants. It is possible that the reason for the failure of prostatic epithelium to stimulate bone formation in connective tissues is the difficulty in dissociation of the epithelium from its stroma, and it is known that the stroma of the bladder will not ossify in the presence of regenerating epithelium of the bladder.

This study indicates also the nonspecificity of periosteum and the osteoblast and that certain other connective tissues under an altered environment may acquire osteogenic properties.

SUMMARY

1. The direct influence of certain epithelial cells on connective tissue stimulating bone formation in it is shown experimentally.

2. Bone forms in a fascial transplant to the bladder of the dog in which the urine has been diverted. It is in close relationship to the epithelium and occurs only in the transplant.

3. Bone forms around a transplant of bladder, ureter and renal pelvis epithelium to certain parietal fascias (rectus sheath, fascia lata, subcutaneous tissue) and to muscle and synovial membrane in the dog. This is true spongy bone with haversian canals containing fibrous and hemopoietic bone-marrow.

4. These fibrocytes can be differentiated functionally from other fibrocytes (those which form around an epithelial transplant from the urinary tract into the kidney, liver and spleen, and those forming from the connective tissue of the wall bladder) which appear anatomically similar but do not participate in the formation of bone.

5. Transplants of the epithelium of the bladder to the sheath of the rectus abdominis fascia in the rabbit did not lead to bone formation,

36. For a complete description of this process, see Phemister, D. B.: The Nature of Cranial Hyperostosis Overlying Endothelioma of the Meninges, Arch. Surg. **6**:554 (March) 1923.

except in one animal. This fascia also therefore can be differentiated from the connective tissue about the renal pelvis, which after ligation of the renal vessels proliferates and forms new bone. Viosterol and parathormone do not aid in ossification in epithelial transplants to the rectus sheath in rabbits.

6. It is the newly formed epithelium and not the nonproliferating part of the transplant that is the essential factor in this osteogenesis.

7. A secretion of fluid containing a relatively large amount of calcium and phosphorus occurs into epithelial-lined cysts of the mucosa of the bladder in the rectus sheath of the dog. It is a probable factor in bone formation.

8. Osteogenesis does not occur following similar transplantation of gallbladder, gastric, jejunal and prostatic epithelium into fascia.

9. Since the osteogenetic power of the mucosa of the renal pelvis has been demonstrated, it is most probable that this is the factor causing bone formation after ligation of the renal pedicle in the rabbit's kidney, especially since this rarely occurs following ligation of the ureter.

THE ASSOCIATION OF RAYNAUD'S DISEASE WITH CEREBRAL SYMPTOMS

REPORT OF A CASE WITH MIGRAINE, PSYCHONEUROTIC SYMPTOMS, TRANSIENT HEMIPLEGIA AND DEATH *

LOUIS CARP, M.D.
NEW YORK

In 1862, Raynaud [1] described the disease which bears his name. It is characterized by attacks of vasomotor and trophic disturbances in which local syncope (blanching) may be followed by local asphyxia (cyanosis) in peripheral portions of the body which may or may not be symmetrical. Paresthesias usually accompany these symptoms and signs. Despite the lack of vascular occlusion, peripheral gangrene is common. The disease is more frequent in neuropathic young women than in men. In a carefully studied history, psychic trauma or prolonged exposure to cold often suggests a not improbable etiologic influence. The symptom-complex, with varying characteristics, may continue intermittently over a number of years. According to Raynaud [1] and Buerger,[2] mild sensory disturbances are usually present, and hemoglobinuria, arthropathies and cerebral symptoms are sometimes observed. Differential diagnosis, not infrequently difficult, is also classified by Buerger.[2] In this paper the cerebral phenomena of Raynaud's disease will be considered.

Based on a review of the literature, the cerebral symptoms associated with Raynaud's disease may, in the main, be divided into the following groups: (1) central vascular manifestations—vertigo, headache, unconsciousness, aphasia, paralysis, convulsive seizures, etc.; (2) mental manifestations—psychoses and psychoneuroses of various types.

The following case, referred to me by Dr. N. E. Broder for surgical opinion, is reported in order to bring out the association of psychic symptoms, attacks of migraine and transitory hemiplegia in a patient in whom a clinical diagnosis of Raynaud's disease was made.

REPORT OF CASE

History.—G. S., aged 26, single, a Jew, who was born in Austria but who had lived in the United States twenty-three years, in the advertising business, presented himself on June 19, 1929, with the following history. The chief complaint

* Submitted for publication, Sept. 23, 1930.

1. Raynaud, A. G. Maurice: De l'asphyxie locale et de la gangrène symétrique des extrémites, Thèse, Paris, 1862.

2. Buerger, Leo: The Circulatory Disturbances of the Extremities, Philadelphia, W. B. Saunders Company, 1924.

was pain at the tip of the right index finger of eight weeks' duration. His father died at 62 of arteriosclerosis; his mother was diabetic and neurotic; two brothers and one sister were in good health and another sister had myxedema. The patient had had measles at 4; he had fallen, hitting the back of his head ten years before presentation. He attributed a partial loss of vision in his left eye, which had developed six years before, to this accident. At this time he was seen by Dr. Ernst Waldstein, who found a slight myopia of the right eye and an old detachment of the lower half of the retina of the left eye. In October, 1925, and January, 1929, Dr. Waldstein found the ocular picture unchanged. He had a fairly constant dry (cigaret?) cough for about three years, with frequent pains in the chest following exposure to cold. There was no fever. It is of interest that ten years before he fainted momentarily while walking in the street. He had always been very nervous.

He said that he had never had a venereal disease. He was a heavy cigaret smoker, and since his present trouble began had smoked about thirty cigarets a day. He indulged moderately in tea and coffee, but abstained from alcohol and drugs. In the past year he had shown a definite decline in business capacity.

The present illness began three or four months before he consulted me, when the patient noticed occasional blueness and coldness in the tip of his right index finger. About eight weeks before, he was bitten on the tip of this finger by a child. Soon afterward he began to have pain, swelling and tenderness in this region, for which he used hot soaks and ointments, without relief. About a week before I saw him his family physician removed the distal third of his nail, and a few days later he went to the Vanderbilt Clinic, where, under block anesthesia, the remainder of the nail was removed. It was found to be brownish and loose, and in the subungual space there were dark, unhealthy granulations and some dark blood, but no pus. The next day the intern noted clotted dark blood at the end of the finger. The roentgenogram showed no involvement of the bone. At my office two days later, the following additional history was obtained. The pain in his finger was becoming more intense, and it seemed to spread to his right hand and forearm. It became almost unbearable at night. Dependent position of the right upper extremity seemed to relieve the pain, but after this position was assumed for some time the distal part of the extremity became swollen. There was no fever or chills. He complained especially of temporal headaches on the right side which were quite severe, and which had shown remissions in the past three years. He became depressed and introspective; he had been worried about the future for some time, because he could not seem to get into his occupational stride. He had tried hard to combat a tendency to neuroticism, and he felt that he was becoming a financial burden to his family.

Examination and Course.—The patient was in great pain. On the dorsal, distal, phalangeal region of the right index finger, in the region of the nail-bed, there was a dark, bloody, sluggish, granulating area extending underneath the eponychium, the paronychium and the distal aspect of the finger. The skin of the right hand was slightly cooler than that of the left, but the pulses were equal and regular. From June 19 to July 1, 1929, hot soaks and codeine gave him some relief, but for the most part the pain in the right upper extremity was becoming more severe. Gradually a line of demarcation at the end of the right index finger formed, involving the nail-bed, eponychium, paronychium and most of the distal anterior closed space. It was difficult for the patient to obtain sleep because of the pain; his appetite was poor, and he was rapidly losing weight.

On July 5, 1929, at 7 a. m., he complained of severe headache and pain around the right eye, and asked his brother for a cold application to his head. A few moments later the brother found the patient on the floor, semiconscious and with an apparent paralysis of the left half of the body. A local physician, called immediately, said the patient had a "stroke of apoplexy" and gave a hypodermic injection of morphine. When I saw the patient three hours later he was conscious, recognized people and objects, and presented a typical left hemiplegia. He complained bitterly of frontal and temporal headache on the right side. The local surgical condition presented a more marked line of demarcation, and, strangely enough, palpation of the radial and brachial pulses on the same side failed to elicit any pulsation. The right radial and brachial arteries felt like hard cords under the finger, but the left were normal. The patient was immediately transported by ambulance to the Harkness Pavilion of the Presbyterian Hospital.

Examination here revealed the following: The respirations were quiet and slow (18) and a full pulse was felt on the left side (110), but there were no palpable pulsations in the right upper extremity. The temperature was 99 F. There was asymmetry of the face and left facial paresis. The mouth contained unswallowed, recently eaten food, and the tongue was deviated slightly to the left. The pupils were equal and reacted to light. The lungs were normal, and although the heart sounds were faint they were of normal rhythm and there were no murmurs. The abdomen was heavily muscled and scaphoid; there were no masses or tenderness. The bladder was distended.

There was a flaccid left hemiplegia. The knee, achilles and triceps reflexes were present on both sides but were greater on the left. The right abdominal reflexes were present, the left absent. There was complete sensory loss on the entire left side. The right hand was slightly colder than the left, but the color of the skin was good and the same on both hands.

On July 5, at 12 noon, the blood pressure was 110 systolic and 80 diastolic; at 9:50 p. m., the systolic pressure was 140 and the diastolic 95. At this time the radial pulse could be felt. Examination of the blood showed: hemoglobin, 70 per cent; red blood cells, 4,500,000; white blood cells, 19,400; polymorphonuclears, 88; lymphocytes, 6; monocytes, 6. The specific gravity of the urine was 1.018; the reaction was alkaline, there was a faint trace of albumin and no sugar. There were few leukocytes and epithelial cells. The Wassermann reaction was negative.

On July 6, during the early morning hours, the patient was conscious but confused. He took fluids and food with difficulty. Hiccup was present. At 9 a. m., he was conscious, and the hemiplegia was still present. The right radial and brachial pulsations were absent. The pain in the region of the right temple and eye was increasing.

At 10 a. m., Dr. Hubert S. Howe was called in neurologic consultation. Pulsation in the right brachial artery down to antecubital space could be seen and felt. There was occasional pulsation in the right radial artery. A complete neurologic examination was impossible because of the mental condition of the patient. There was a left, flaccid hemiplegia, with involvement of the face, tongue, arm, hand and lower extremity. The abdominal reflexes were absent on the left and active on the right. There was a Babinski sign on the left and a questionable one on the right. There was left hemianesthesia.

At 11 a. m., the patient began moving the left extremities, which had remained paralyzed until then.

At 1 p. m., he became unconscious and could not be aroused. He was moving all his extremities freely, and the left upper extremity was then so strong and active that a venous puncture could not be done on this side. The respirations

were stertorous and labored. Over the left side of the chest were coarse rolling râles with inspiration. He became paler and slightly cyanotic. The corneal reflexes were absent. The heart sounds were normal. The eyeground was normal in the right eye, and in the left there was a detachment of the retina on the temporal side. The rest of the retinal field was pale. The vessels on the left were smaller than those on the right.

At 4 p. m., the patient was definitely worse. He was still unconscious, and vomitus had to be cleared from his mouth. He suddenly became more cyanotic and ceased breathing, but the pulse continued rapid and palpable for several minutes. Stimulants, intravenous infusion of dextrose and the pulmotor did not prevent death, which was probably caused by asphyxia due to aspiration of vomitus.

During his twenty-nine hours of hospitalization, he voided 1,100 cc. of urine.

A postmortem examination could not be obtained.

REVIEW OF LITERATURE

Raynaud himself described cases with cerebral involvement. In one instance, a woman of 62 had transient hemiplegia two years before the onset of symmetrical gangrene. In the third case that he describes, there was paralysis of the right arm. Up to 1916, Monro,[3] Osler [4] and Norman [5] made observations in this connection, and the reader is referred to their work for more detailed references in the literature. Since that time there have appeared articles describing many bizarre neurologic manifestations in Raynaud's disease (Weeks and Renner,[6] Hollis,[7] Ward,[8] de Forest,[9] Sieben [10]).

Monro said:

> Nearly one-fourth of all patients with Raynaud's disease are reported to suffer or have suffered in the past from phenomena related to disturbances of the nervous system. . . . Five per cent had convulsions at some time or another and others have had diseases such as congestion of the brain, general paralysis, etc. . . . The patient may be a regular epileptic in whom Raynaud's phenomena began about the same time as or many years after the fits.

3. Monro, Thomas Kirkpatrick: Raynaud's Disease, Glasgow, James Maclehose & Sons, 1899.

4. Osler, William: The Cerebral Complications of Raynaud's Disease, Am. J. M. Sc. **112**:522, 1896.

5. Norman, Hubert J.: The Cerebral Associations of Raynaud's Disease, Lancet **2**:1049 (Dec. 23) 1916.

6. Weeks, David F., and Renner, Dan S.: A Case of Symmetrical Gangrene or Raynaud's Disease Associated with Epilepsy, J. A. M. A. **66**:651 (Feb. 26) 1916.

7. Hollis, K. E.: Raynaud's Disease of Four Years' Duration: Acute Fatal Termination with Signs of Involvement of Arteries of Central Nervous System, Canad. M. A. J. **12**:108, 1922.

8. Ward, E. H. P.: Manic Depressive Insanity and Raynaud's Disease, M. Rec. **97**:694 (April 24) 1920.

9. de Forest, Henry P.: Raynaud's Disease, J. M. Soc. N. J. **17**:181, 1920.

10. Sieben: Raynaudische Krankheit und Hysterie, Med. Klin. **15**:712, 1919.

According to Osler, there are no features of Raynaud's disease suggestive of coarse lesions of the central nervous system. There is a surprising paucity of autopsy reports in the literature to prove clinical interpretations. In one instance, reported by Wigglesworth,[11] an insane woman, also epileptic, who had Raynaud's symptom-complex, died suddenly after a fit. At autopsy, the pia was slightly thickened, and the brain, cord and peripheral nerves were normal to the naked eye. Microscopically, the spinal cord was normal. The peripheral nerves showed "degeneration of nervous elements and overgrowth of fibrous elements." The epineurium and perineurium were thickened.

SUMMARY AND COMMENT

The patient whose case is reported was a 26 year old Jew, single, born in Austria, who had lived in this country for twenty-three years. He came from a neurotic family. Six years before the onset of his present illness, he suffered from progressive loss of vision in the left eye which was caused by partial detachment of the retina. For three years he had intermittent migrainous attacks on the right side. He had been discouraged by his prospects in life for several years, and could not seem to make any headway, although intelligent and educated. Several months previously he observed a transient coldness and blueness at the tip of his right index finger; eight weeks previously this part of his finger had been bitten by a child. Thereafter he developed progressive dry gangrene of the tip of this finger accompanied by severe pain. On the morning of admission to the hospital, after an attack of severe temporal headache on the right side, he suddenly had a left hemiplegia. For the first time the pulsations of the radial and brachial arteries on the affected extremity could not be felt, and the vessels felt like hard cords. In the course of the next twenty-four hours, his pulses could be felt at times. Twenty-eight hours after the inception of his hemiplegia, the paralysis disappeared. He then became unconscious and after progressive cyanosis and stertorous respirations, he suddenly became deeply cyanotic and died in a few minutes—thirty-three hours after the hemiplegia began—probably from asphyxia due to aspiration of vomitus.

Clinically, this patient had Raynaud's disease, with psychic symptoms and several migrainous attacks on the right side over a period of several years. A sudden onset of hemiplegia, contralateral to the extremity involved and to the side on which he had temporal headache, accompanied by intermittent pulsations of the radial and brachial arteries which could be felt on the affected extremity, together with the subsequent

11. Wigglesworth, J.: Peripheral Neuritis in Raynaud's Disease (Symmetrical Gangrene), Tr. Path. Soc. London **38**:61, 1887.

disappearance of the paralysis, point to one etiologic factor—transient peripheral and cerebral angiospasm.

It is now known that cerebral blood vessels in mammals have vasomotor control (Forbes and Wolff,[12] Kennedy,[13] Meagher and Ingraham,[14] Talbott, Wolff and Cobb[15]). Further, Hiller and Grinker[16] stated: "The etiology of many obscure transient nervous syndromes . . . without apparent organic cause may be solved by further study of the possibility of functional circulatory disturbances."

A review of the literature shows that the cerebral symptoms of Raynaud's disease are more frequent than is the usual impression, and that the manifestations may be central, vascular or mental. These may precede the obvious clinical syndrome by varying periods of time.

---

12. Forbes, Henry S., and Wolff, Harold G.: Cerebral Circulation: III. The Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928.

13. Kennedy, Foster: Epilepsy and the Convulsive State, Arch. Neurol. & Psychiat. **9**:567 (May) 1923.

14. Meagher, R. H., and Ingraham, F. D.: The Relation of the Cervical Sympathetic Trunk to Cerebral Angiospasm, Arch. Neurol. & Psychiat. **22**:570 (Sept.) 1929.

15. Talbott, John H.; Wolff, Harold G., and Cobb, Stanley: The Cerebral Circulation: VII. Changes in Cerebral Capillary Bed Following Cervical Sympathectomy, Arch. Neurol. & Psychiat. **21**:1102 (May) 1929.

16. Hiller, Friedrich; and Grinker, Roy R.: Functional Circulatory Disturbances and Organic Obstruction of the Cerebral Blood Vessels, Arch. Neurol. & Psychiat. **23**:634 (April) 1930.

TUBERCULOSIS OF THE STOMACH

AN ANALYSIS OF CASES RECENTLY REVIEWED *

RALPH W. GOOD, M.D.
CINCINNATI

INCIDENCE

From available material it was difficult to determine how frequently tuberculosis of the stomach occurs. Data collected from various sources are given in table 1. There were even fewer data available on which to base an idea of the frequency of the lesion as found at operation on the stomach. At the Mayo Clinic it occurred in 0.035 per cent of the total number of 7,416 gastric operations. Clairmont's [1] report included 2 tuberculous stomachs in 258 gastric operations (0.80 per cent), and Demel's [2] report included 3 in 1,568 (0.19 per cent). In the data from the Mayo Clinic and the articles just cited, the combined incidence of tuberculosis of the stomach, as discovered at operation, was 0.34 per cent. The average incidence as derived from the total number of necropsies also was 0.34 per cent.

Tuberculosis of the stomach has been known as a disease of the adult male. It has been believed to affect adults and children in the ratio of 3:1. The ratio of male to female has been recorded as high as 5:1 by Melchior, and according to Gossmann and Broders,[3] respectively, the ratio is 2.6:1 and 2:1.

PROTECTIVE MECHANISM OF THE STOMACH

Why any segment of the gastro-intestinal tract should be unequally affected by tuberculosis remains as yet unexplained. In theory, biologic factors involved in the protective mechanism of the stomach against the bacillus of tuberculosis include: (1) normal gastric juice, (2) intact mucous membrane, (3) paucity of lymph follicles in the gastric wall and (4) normal muscular action.

---

* Submitted for publication, May 17, 1930.

* Abridgment of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Surgery, December, 1929.

1. Clairmont, Paul: Bericht über 258 von Prof. von Eiselsberg ausegeführte Magenoperation, Arch. f. klin. Chir. **76**:180, 1905.

2. Demel, Rudolf: Zur Pylorusstenose auf tuberkulöser Basis, Deutsche Ztschr. f. Chir. **183**:348 (Dec.) 1923.

3. Broders, A. C.: Tuberculosis of the Stomach with Report of a Case of Multiple Tuberculous Ulcers, Surg. Gynec. Obst. **25**:490 (Nov.) 1917.

MODES OF INFECTION; LESIONS

Modes of Infection.—From an academic standpoint, primary tuberculosis of the stomach has yet to be seen. The cases reported as primary suffer the limitations inherent both in clinical examination and in necropsy. Tuberculous lesions of the stomach are as a rule secondary to some other tuberculous focus in the body, for instance a focus in the lung or in the intestine.

Both experimental and pathologic material leave the question of the mode of infection indeterminate among several possibilities. The blood

TABLE 1.—*Incidence of Tuberculosis of the Stomach Noted at Necropsy*

Author	Total Necropsies	Percentage	Necropsies in Tuberculous Subjects	Percentage	Tuberculous Stomachs
Claytor and Wilkinson, quoted by Sappington: Hahneman. Month. **55**: 227, 1920	7,169	0.70	.....	.....	50
Eisenhardt, quoted by Baetzner: Berl. klin. Wchnschr. **57**: 1237, 1920	.....	....	6,000	0.016	1
Glaubitt, quoted by Zesas: Centralbl. f. d. Grenzgeb. d. Med. u. Chir. **16**: 448, 1913	12,528	0.37	2,237	2.10	47
Gossmann: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **26**: 771, 1913	5,900	0.30	2,360	0.80	18
Grusdew, quoted by Zesas: Centralbl. f. d. Grenzgeb. d. Med. u. Chir. **16**: 448, 1913	18,593	0.12	.....	.....	23
Heubschmann: Pathologische Antomie der Tuberkulose, Berlin, Julius Springer, 1928, p. 300	10,000	0.10	.....	.....	10
Kundrat, quoted by Zesas: Centralbl. f. d. Grenzgeb. d. Med. u. Chir. **16**: 448, 1913	.....	....	418	0.48	2
Letulle, quoted by Zesas: Centralbl. f. d. Grenzgeb. d. Med. u. Chir. **16**: 448, 1913	.....	....	180	0.55	1
Meichlor, L.: Beitr. z. Klin. d. Tuberk. **26**: 2, 1913	.....	0.70	848	.....	6
Ophüls: A Statistical Survey of Three Thousand Autopsies, Stanford University, Stanford University Press, 1926, vol. 1, p. 144	3,000	0.00	632	0.00	0
Orsós: Deutsche Ztschr. f. Chir. **191**: 306 (June) 1925	6,280	0.08	.....	.....	5
Plambeck, quoted by Biernath: Deutsche med. Wchnschr. **47**: 1091, 1921	.....	....	490	0.60	3
Robertson, H. E.: Personal communication to the author	8,401	0.00	.....	0.00	0
Simmonds: München. med. Wchnschr. **47**: 317, 1900	.....	....	2,000	0.40	8

stream as a route is more generally favored than the lymph stream. Infection by ingestion or spread by continuity or contiguity with adjacent tuberculous organs at times can be demonstrated.

Lesions.—Excluding in tuberculous subjects diffuse, generalized, nonspecific inflammations, mucosal erosions and generalized miliary tuberculosis of the stomach, there remain to interest the surgeon the more focal tuberculous lesions associated with ulcer, tumor, scarring and their combinations.

The tuberculous ulcer predominates; it can be single or multiple, varying in diameter from a few millimeters to as much as 10 cm. In its typical although infrequent form, the ulcer presents undermined, ragged edges and a dirty, grayish-yellow base, covered at times with

visible tubercles. It usually does not extend more deeply than to the muscle layer. Perforation seemingly is its least characteristic feature. Hemorrhage from the ulcer is not so uncommon. The situation of the ulcer usually is along the lesser curvature in the pyloric end of the stomach, with a tendency toward appearing on the posterior wall.

The chief characteristic of the tumor is its mass, often associated with an ulcer. At times there is early caseation and liquefaction under the intact mucous membrane and production of an abscess of the gastric wall. The abscess may rupture in sievelike fashion into the lumen of the stomach to form multiple ulcers, or interstitial cavernous gastritis. Cirrhosis and cicatrization are the earmarks of the scar form. This and the tumor form also are found most often in the pylorus.

With a tuberculous lesion of the stomach there is commonly early involvement of regional lymph nodes and a tendency to early caseation. In practice, perhaps because of unfamiliarity, there is little concerning the gross appearance of a gastric lesion that would mark it as tuberculous unless tubercles were visible. The nature of the lesion is established only by microscopic examination. The microscopic tubercles are most numerous about the muscularis mucosae. Demonstrating the organisms with proper stains is tedious and difficult.

ASSOCIATION OF GASTRIC ULCER, CARCINOMA AND TUBERCULOSIS

Tuberculosis of the stomach mimics and is always confused with the signs and symptoms of gastric ulcer, carcinoma or their complications.

The coincidence of gastric carcinoma and gastric tuberculosis was observed by Faltin [4] only twelve times. In a man 62 years of age, with tuberculosis of the apex of the right lung, he found adenocarcinoma in a tuberculous ulcer. Anschütz and Konjetzny [5] found a single tubercle in the margin of a gastric carcinoma, and in the regional lymph nodes there were both carcinomatous metastasis and caseous tubercles.

An organic gastric lesion, associated with pulmonary tuberculosis, is almost bound to be a gastric ulcer or a carcinoma; therefore, the patient, unless he is in the terminal stage of tuberculosis, should be accorded abdominal exploration. During the period in which the two reported cases occurred at operation at the clinic, 2,963 operations were performed on the stomach for carcinoma and 1,952 operations on the stomach for ulcer.

---

4. Faltin, R.: Simultaneous Occurrence of Tuberculosis and Cancer in the Stomach, Finska läk.-sällsk. handl. **68**:659 (July) 1926; Gleichztiges Vorkommen von Tuberkulose und Carcinoma im Magen, Acta chir. Scandinav. **61**:331, 1927.

5. Anschütz, Willy, and Konjetzny, G. E.: Kombination des Magenkarzinoms mit Magentuberkulose, in: Die Geschwülste des Magens, Deutsche Chir. Stuttgart, Stuttgart, Ferdinand Enke, 1921, 46 f., pp. 240-242.

DIAGNOSIS, PROGNOSIS AND TREATMENT

Diagnosis.—The accurate clinical diagnosis of tuberculosis of the stomach is difficult, if not impossible. There is nothing distinguishing about either the history or the observations on general examination to indicate the tuberculous nature of a gastric lesion. An associated active pulmonary lesion can only arouse suspicion. Tuberculosis of the stomach is met with at operation just as frequently in subjects in whom no other tuberculous focus can be demonstrated. Of the organic defects of the stomach, as revealed by the roentgen ray, none is sufficiently characteristic to furnish a diagnosis of tuberculosis of the stomach. With present methods, the disease will continue to be confounded with gastric ulcer and with carcinoma.

Prognosis and Treatment.—The comfort derived from surgical measures for a tuberculous gastric lesion justifies the risk entailed. When the gastric lesion is the only manifestation of tuberculosis, removal should lead to cure. Tuberculosis of the stomach eventually needs surgical treatment. There seems to be but a feeble tendency to early or complete healing, and in some cases, a rapid tendency to pyloric obstruction. A gastric lesion and its complications in the trials of a patient with pulmonary tuberculosis affect one of the deciding issues, the state of nutrition. If the state of nutrition is maintained, it may make it otherwise possible to arrest or heal the pulmonary lesion under medical treatment. Whatever the surgical procedure may be, it must fit the physical state of the patient. Jejunostomy, gastro-enterostomy and gastric resection have their indications.

MATERIAL

In 1917, Broders published a report of a case of tuberculosis of the stomach in a patient who underwent surgical treatment. He included an analysis of the cases reported until then, and classified them as positive, probable, doubtful and rejected. Since Broder's report, thirty-three additional reports of cases have been reviewed from the literature and two other cases have been seen at the Mayo Clinic. According to the classification which Broders employed in his paper, two of the thirty-five cases which form the basis of my study would qualify as positive cases and twenty-four as probable cases of tuberculosis of the stomach. The remaining nine cases were excluded because they fell into the doubtful or rejected groups or because surgical treatment was not employed. If a histologic picture of tuberculosis is to be acceptable at all, those cases classified as probable on the basis of a microscopic picture of tuberculosis were cases of tuberculosis of the stomach.

The twenty-six cases (table 2) which remained after nine of the thirty-five had been excluded were subjected to analysis in the hope

that through recent refinement in both clinical and laboratory methods of examination some criteria could be found which would aid in clinical recognition of the gastric lesion.

The sexes were about evenly represented; in the twenty-five cases in which sex was noted, thirteen were males and twelve were females.

TABLE 2.—*Source of Case Reports*

	Probable Cases
Albu, in: Spezielle Pathologie und Therapie innerer Krankheiten, Berlin, Urban & Schwarzenberg, 1921, vol. 5, p. 993	1
Baetzner: Berl. klin. Wchnschr. **57**: 1237, 1920	1
Bertoloni: Osp. maggiore **9**: 197, 1921	2
Biernath: Deutsche med. Wchnschr. **47**: 1091, 1921	1
Demel	2
Faltin	1
Friedman, G. A.: J. A. M. A. **72**:101 (Jan. 11) 1919	1
Hartmann and Renaud: Bull. et mém. Soc. anat. de Paris **90**: 357, 1920	1
Höfer: Beitr. z. klin. Chir. **126**: 555, 1922	1
Hurst: Guy's Hosp. Rep. **75**: 428 (Oct.) 1925	1
Mayo Clinic	2
Melchior, E.: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **39**: 205, 1926	5
Orsós	1
Razzaboni: Policlinico (sez. chir.) **26**: 153, 1919	1
Rother: Berl. klin. Wchnschr. **55**: 1049 (Nov.) 1918	1
Severin: Berl. klin. Wchnschr. **54**: 738, 1917; Deutsche med. Wchnschr. **52**: 1168, 1926	1
Spengler: Med. Klin. **17**: 101 (Jan. 23) 1921	1
Suermondt: Nederl. Tijdschr. v. geneesk. **1**: 2309, 1925; abstr., J. A. M. A. **85**: 236 (July 18) 1925	1
Willerding: Arch. f. klin. Chir. **128**: 109, 1924	1
Total	26

TABLE 3.—*Symptoms and Signs of Tuberculosis of the Stomach*

Symptoms and Signs	Present, Cases	Absent, Cases	Not Recorded
Pain, after food	24	..	2
Loss of weight and strength	23	..	3
Vomiting	19	3	4
Free hydrochloric acid	15	7	4
Tuberculosis elsewhere	12	12	2
Palpable tumor	9 (3?)	11	3
Hemorrhage:			
From mouth	3	8	10
From bowel	5		
Constipation	8	3	15
Diarrhea	4	5	17

The ages ranged from 18 to 62 years, and averaged about 38½ years. The third decade of life was represented by the greatest number.

The gastric symptoms and signs (table 3) were present for periods varying from three weeks to sixteen years, and averaged close to two years. The most constant symptoms were epigastric pain after meals, loss of weight and strength and vomiting. Epigastric pain after eating was present in twenty-four cases. In twenty-three cases in which loss of weight and strength were mentioned, they were recorded as being present. In twenty-two cases, vomiting was recorded as present in nineteen (86 per cent) and as absent in three. In the total of twenty-

six cases, hemorrhage from the mouth was recorded three times, and from the bowel, five times. Constipation and diarrhea, judging from the number of times that they were not mentioned, seemingly were of little significance, but constipation was mentioned a few more times than diarrhea. In twenty-two cases, free hydrochloric acid was recorded as present in fifteen (68 per cent) and as absent in seven. In the series it ranged from 0 to 65, and averaged about 16.

The preoperative diagnosis included gastric ulcer in eight cases, gastric carcinoma in four and pyloric obstruction in six. Tuberculosis of the stomach was thought of but once. In six of the cases in which the diagnosis was combined ulcer and pyloric obstruction, the presence of a malignant lesion could not be ruled out.

Nine (39.1 per cent) of twenty-three cases presented definite tumors on palpation in the upper part of the abdomen, three (13.1 per cent) had questionably palpable tumors and eleven (47.8 per cent) did not present a mass.

In twelve of twenty-four cases, there were manifestations of tuberculosis elsewhere in the body. In cases in which tuberculosis was present elsewhere, pulmonary lesions were represented in 100 per cent. Besides pulmonary involvement, in one case there were lesions of bone and in another, tuberculous epididymitis.

In twenty (77 per cent) of twenty-six cases, roentgenologic examination revealed some sign of organic gastric defect. Hour-glass deformity was represented in two cases.

Radical surgical treatment predominated. In twenty cases (77 per cent) some type of gastric resection was done: the Billroth II type of anastomosis was done in ten cases and the Polya type in two; excision of the lesion, combined with gastro-enterostomy, was done in two, a Kocher gastroduodenostomy was done in one case and the type of resection was not recorded in five cases. Gastro-enterostomy alone was done in five cases and biopsy alone in one case.

Concerning the possibility of recognizing the lesion at the time of operation, tuberculosis was mentioned in only one case, a case in which tubercles were visible. The nature of the lesion was surmised in three cases; in two cases the lesion was called carcinoma and in two it was questioned as being carcinoma.

Of the twenty-four cases in which the result is known, nineteen (79 per cent) patients survived the operation and five (21 per cent) died. Two patients were alive and well, respectively, three and a half and ten years after operation. Both were operated on for carcinoma of the stomach; in neither case was there clinical evidence of tuberculosis elsewhere in the body. There were two deaths, respectively, in one month and in two and a half years after operation, both from tuberculosis.

The tuberculous gastric lesions in the twenty-six cases were as follows: ulcer only, ten cases; tumor and ulcer, ten; tumor only, three; miliary only, two, and miliary with tumor, one case.

The parts of the stomach involved included the pylorus in seventeen cases, the lesser curvature in nine cases, the posterior wall in seven cases, the anterior wall in four cases and the greater curvature in two cases.

REPORT OF CASES

CASE 1.—A man, aged 40, presented himself at the Mayo Clinic on Feb. 1, 1927, complaining of pain in the stomach and of abdominal distention. He had been married for seven years; his wife and two children enjoyed good health. For the five years before he came to the clinic he had had a periodic, continuous, gnawing epigastric pain, aggravated by the taking of food, and lasting from one to two weeks, with respites of from two to three months. When the pain had been present, the epigastrium had been sore to the touch. After two years, the pain had increased in severity and the attacks had increased in duration sufficiently to become inconvenient and to cause marked failure of the appetite. He had borne the severer spells for another year, and then had sought medical aid. On investigation elsewhere, a gastric ulcer had been diagnosed clinically and had been confirmed roentgenologically. Tonsillectomy and a medical regimen had been carried out with immediate, but temporary, relief. The pain and disability had returned to such a degree that the patient had been confined to bed for intervals of from one to two days. At the time he arrived at the clinic there was no relief from taking food, but some relief from taking sodium bicarbonate; complete relief was always obtained by inducing vomiting. There was no pain at night. Until one year before he came to the clinic his weight had been stationary, but since then he had lost as much as 40 pounds (18.1 Kg.).

General examination revealed a fairly healthy, undernourished-looking man, 5 feet 9¾ inches (176.13 cm.) tall, weighing 106 pounds (48.1 Kg.). The temperature was normal. The heart and lungs appeared to be normal. Abdominal examination disclosed only a palpable, slightly tender mass in the region of the pylorus. The urine was normal to examination; the concentration of hemoglobin was 76 per cent; leukocytes numbered 5,300 in each cubic millimeter of blood. Analysis of the gastric content disclosed total acidity equivalent of 56 (5.6 cc. of tenth-normal sodium hydroxide neutralized 10 cc. of filtered gastric content). The free hydrochloric acid was estimated as 40. The quantity of gastric content recovered was 120 cc. The Wassermann reaction of the blood was negative. Roentgenologic study of the thorax gave negative results on two occasions. The gallbladder appeared to be normal on roentgenologic examination, but the gastric roentgenoscopic examination revealed a small ulcer, interpreted as benign, situated on the lesser curvature at the angle of the stomach.

Exploration of the ulcer was advised and was done on February 10. Along with an ulcer at the middle of the lesser curvature of the stomach was a large, infiltrating, indurated area in the gastric wall associated with a large number of hard, enlarged lymph nodes in the lesser omentum. Several of the latter were removed for examination. Partial gastrectomy with a Billroth II type of anastomosis was done.

In the resected portion of the stomach there was an apparently inflammatory lesion and a superficial ulcer without a crater. The lymph nodes also, to all appearances, were inflammatory. Microscopically, both the gastric lesion and the

lymph nodes presented the picture of tuberculosis. The mucous membrane generally was intact, but it displayed a rich, lymphocytic cellular reaction, with scattered foreign body giant cells, with and without the formation of tubercles. The lymph follicles were not involved. The submucosa was thick and compact and gave evidence of hyaline changes. It also contained tubercles of typical structure within its upper half, toward the muscularis mucosae. There were many congested blood vessels surrounded by lymphocytic infiltration. The muscle layer was swollen and hyalinized, and there was some increase of connective tissue and cellular reaction. The predominating reacting cells were lymphocytes, but near the serosa there were regions of polymorphonuclear cells. The organisms were sought for but were not found.

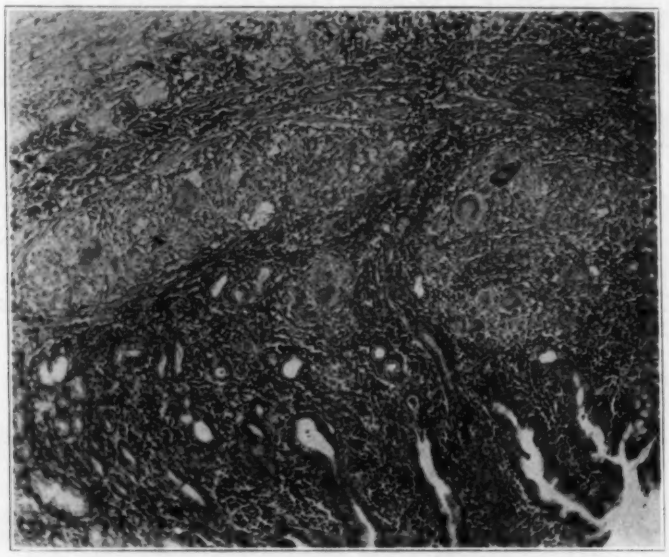


Fig. 1 (case 1).—Typical tubercle formation at the muscularis mucosae; × 75.

The postoperative convalescence was uneventful. Examination, on October 31, revealed that the only complaint was of gas and discomfort in the abdomen associated with overeating and the ingestion of milk. The weight was 112¾ pounds (51.1 Kg.). The urine again was normal; the concentration of hemoglobin was 74 per cent. Many blood cell counts were within normal limits. Analysis of the gastric content disclosed achlorhydria, and a total acidity of 22; bile was present in abundance. Again the thorax did not present clinical signs of tuberculosis. Roentgenograms of the colon gave evidence of normal conditions; those of the stomach indicated that the lumen at the point of gastro-enterostomy was free.

The patient was well in July, 1929, but was somewhat underweight and nervous.

Case 2.—A man, aged 56, presented himself at the clinic on June 28, 1928, complaining of his stomach. One of his sisters had died of tuberculosis at the age of 40. His wife and daughter were in good health. At the age of 9 years he had had scrofula, which had manifested itself in the spinal column and right

groin. At the ages of 27 and 42, he had had sieges of illness called typhoid fever. Between the ages of 40 and 46 he had begun to have periodic attacks of epigastric pain coming on late after meals; these attacks occurred for six weeks at a time in warm weather. At the age of 44, in the course of one of his attacks, he was seized with an agonizing epigastric pain. Operation was performed immediately. Afterward he was told that he had had a perforating gastric ulcer, which had been closed. His previous disability soon returned and was complicated by vomiting. Five years later, during an attack, he experienced great weakness and loss of weight; at one time, a hemorrhage from the stomach had resulted in loss of a quantity of blood estimated to be at least a liter. He had submitted to a medical regimen, and his condition had begun to improve at once. He had vague recollections of having had slight epigastric discomfort since then, during the summer. There had been no pain at night; overwork and riding in the saddle had caused the distress to return. From October to December, 1927, he had felt well for the first time in years. Then he had begun to note, in the mornings, a sensation as if a ball were rolling around in his stomach. Riding in the saddle had begun to nauseate him, and he had begun to lose appetite and also weight. Bloating, belching and vomiting, of food eaten as long as twelve hours before, had set in. On one occasion there again had been blood-tinged vomitus; in two months the patient had lost 15 pounds (6.8 Kg.).

General examination revealed an emaciated, dehydrated man, 5 feet 5½ inches (166.37 cm.) tall, weighing 127 pounds (57.6 Kg.). There was marked dorsal scoliosis and kyphosis, with small, crusted, superficial ulcers over the bony prominences of the back. Examinations of the heart and lungs did not give significant results, except for the marked thoracic deformity. The abdominal organs apparently were normal. There were scars marking the site of the scrofula in the groin and an incisional scar on the abdomen. Analysis of gastric content disclosed a total acidity of 50 and free hydrochloric acid of 34. Blood was present in the aspirated content. The Wassermann reaction of the blood was negative. Urinalysis, except for an occasional pus cell, disclosed normal conditions. The concentration of hemoglobin was 74 per cent; the leukocytes numbered 4,200 in each cubic millimeter of blood. Roentgenologic examination of the thorax gave evidence of old pleuritic adhesions to the right side of the diaphragm, old destructive arthritis of the tenth and eleventh thoracic vertebrae, with fusion, and marked angulation of the spinal column. The interpretation of the gastric study was that there was an ulcer, probably malignant, on the posterior wall of the stomach at the angle. A preoperative diagnosis of probable carcinoma superimposed on a gastric ulcer was made, and exploration of the lesion was advised.

The patient was hospitalized for the purpose of feeding him and building up his ability to take fluid. Operation was done on July 3, 1928. Well around on the anterior aspect of the stomach was a fine, white line that was taken to be the mark of previous closure of a perforation. Above this line, and extending posteriorly, an ulcer, with a crater 2 cm. in diameter, was palpable. Even though the stomach was adherent posteriorly, the only advisable procedure seemed to be resection of the stomach. About half of the organ was removed, and a posterior type of Polya anastomosis was made. The resected specimen presented marked thickening, induration and unevenness of the gastric wall, together with an ulcerated area 2 cm. in diameter, with no distinguishing marks.

Microscopic examination of the gastric wall and of the lymph nodes attached in the omental tags disclosed a tuberculous process. All the layers of the stomach were greaty thickened. The mucosa, where it was intact, seemed swollen and richly invaded by lymphocytes. The lymph follicles were large, the germinal

centers were thin and the denser peripheral zones were irregularly drawn out, far toward the surface of the mucous membrane; the follicles were free from involvement by tubercles. Beneath the muscularis mucosae, tubercles with and without giant cells appeared as large clear whorls, with a very slight lymphocytic reaction about them. The submucosa was greatly thickened by an increase in the hyalinized fibrous tissue. The blood vessels were large, fairly numerous and distended. There was an occasional small, free hemorrhage. In the entire layer, there was an absence of cellular reaction. The hyaline-like muscle layer presented swollen bundles of muscle fibers widely separated as much by edema as by an increase of connective tissue. The serosa was approximately twice as thick as the layer of muscle; it was edematous, and was rich in hyalinized fibrous tissue. The blood vessels were congested and one vessel was thrombosed. There were no tuberculous formations near it. Along the edge of the ulcer, where the mucous membrane

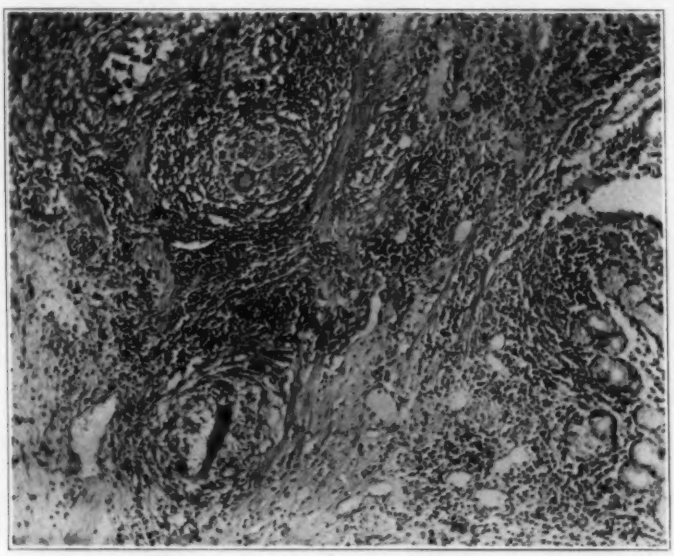


Fig. 2 (case 2).—Tubercle formation along the muscularis mucosae; × 75.

was still recognizable but not intact, typical tubercles, with rich polymorphonuclear exudate, were present. The necrotic center of the ulcer went through to the layer of muscle. For a wide margin about the necrotic area there was an extremely dense eosinophilic cellular reaction, which at points where the ulcer and muscle came in contact extended throughout the layer of muscle. The necrosis in the bed of the ulcer did not appear to be caseation necrosis. Nothing resembling tubercles was noted in its vicinity. The regional lymph nodes were all but replaced by noncaseating tubercles; the germinal follicles were uninvolved. Organisms were sought for, but were not found.

The patient died on the seventh postoperative day, from circulatory collapse complicated by diffuse pneumonia.

At necropsy, the major anatomic diagnoses were bilateral, massive, coalescing bronchopneumonia, healed lesions of adhesive pericarditis and pleuropericarditis, healed lesions of tuberculosis of the lungs and spinal column and arteriosclerosis. What seemed to be about a third of the stomach remained and appeared normal.

Microscopic examination of specimens from the lower lobe of the left lung, the spleen, an aortic lymph node and the lesser omentum disclosed more or less typical formation of tubercles.

Comment.—Case 1 is typical of those reported as examples of primary tuberculosis of the stomach. It is the type that lends itself favorably to a good prognosis.

Case 2 presents much evidence of previous tuberculosis elsewhere in the body, arrested, if not healed. There is no evidence on which to base a belief that the long history of gastric disturbance, marked by an acutely perforating ulcer, was caused by tuberculosis of the stomach from the beginning.

The history in each case was fundamentally that of gastric ulcer. There was no difficulty, by clinical and laboratory means, in establishing the presence of a gastric lesion.

SUMMARY AND CONCLUSIONS

Tuberculosis of the stomach is a rare disease of adults. The outstanding elements accompanying the chronic dyspepsia are pain after meals, loss of weight and strength and vomiting. Half of the cases are associated with tuberculosis elsewhere in the body. The disease is mistaken for gastric ulcer or carcinoma. Symptoms of pyloric stenosis are common. The treatment is surgical, and by choice consists of radical resection of the lesion-bearing portion of the stomach. The pyloric end of the stomach is the site of predilection. In most instances, the gross appearance of the lesion, except for the presence of an ulcer, a tumor, scarring or combinations of the three lesions, does not identify itself as tuberculous unless visible tubercles are present. The real nature of the lesion is revealed only by microscopic examination. Bacilli of tuberculosis are difficult to demonstrate in the lesion.

The presence of an organic gastric lesion can be relatively easily established. If surgical treatment is prescribed for all chronic organic gastric lesions, the rare disease of tuberculosis of the stomach does not create a new problem.

In most instances evidence of tuberculosis elsewhere in the body is not a contraindication to exploration of a gastric lesion.

Tuberculosis of the stomach is diagnosed by histopathologic methods. There is no need clinically to differentiate tuberculosis of the stomach from the commoner chronic organic gastric lesions in order to institute the proper treatment.

THE RÔLE OF THE PYLORIC SPHINCTER IN THE BEHAVIOR OF GASTRIC ACIDITY*

ROBERT ELMAN, M.D.
AND
A. P. ROWLETTE, M.D.
ST. LOUIS

It is the purpose of this report to present observations on certain changes in the behavior of gastric acidity which follow experimental diminution in the activity of the pyloric sphincter (pyloric insufficiency). In previous communications [1] from this laboratory experiments were described which indicated that reflux of alkaline pancreatic juice into the stomach was probably an important factor in the regulation of the level of gastric acidity. One might expect as a corollary that the pyloric sphincter governs this regurgitation in a decisive way. Direct roentgenologic observations of such a phenomenon have been made in human beings by Salamond.[2] The present experiments add further support to the theory.

PREVIOUS WORK

That there is a relationship between gastric acidity and the pyloric muscle has long been noted from a great variety of evidence,[3] which need not be reviewed here. A succinct statement of this relationship was advanced in 1907 by Cannon [4] in a theory called the "acid control of the pylorus," which stated that acid, on the stomach side opened, and on the duodenal side closed, the pylorus. On that basis, the gradual emptying of the stomach was explained.

For a great many years this theory was quite generally accepted, and undoubtedly accounts for a good many facts. The theory fails, however, to explain a number of phenomena, many of which Cannon himself called attention to in his original communication. One of the significant objections is that it does not explain how the pylorus opens

* Submitted for publication, May 17, 1930.

* From the Department of Surgery, Washington University School of Medicine and Barnes Hospital.

1. Elman, Robert: Probable Influence of Pancreatic Juice in the Regulation of Gastric Acidity, Arch. Surg. **16**:1256 (June) 1928; Surg. Gynec. Obst. **49**:34, 1929. Olch, I. Y.: Duodenal Regurgitation as a Factor in Neutralization of Gastric Acidity, Arch. Surg. **16**:125 (Jan.) 1928.

2. Salamond, R. W. A.: J. Radiol. **11**:453, 1928.

3. Babkin, B. P.: Aeussere Sekretion der Verdauungsdrüsen, ed. 2, Berlin, Julius Springer, 1928, p. 801.

4. Cannon, W. B.: Am. J. Physiol. **20**:283, 1907.

in patients with anacidity, a condition which we now know is not infrequent in healthy persons. Indeed, in such persons in spite of the absence of acid there is often fluoroscopic evidence of a patulous pylorus and an increased emptying time. Hyperacidity, on the other hand, with or without symptoms, instead of accelerating pyloric opening, is frequently associated with pylorospasm and delayed emptying. It has been repeatedly shown, moreover, in experiments on both laboratory animals and man,[5] that within normal limits the more acid the test solution the more slowly it leaves the stomach. Cannon explained the latter facts by stating that the stronger acid, requiring longer for its neutralization on reaching the duodenum, thus maintains closure of the pylorus and delays emptying. This conception emphasizes the importance and necessity of neutralization of acid but does not support the part of the theory concerned with the rôle of acid on the stomach side in opening the pylorus. The neutralization of acid undoubtedly plays a most decisive rôle, but, as indicated by the evidence already referred to,[1] it probably occurs in the stomach through reflux of pancreatic juice rather than in the duodenum directly.

One of the great difficulties in explaining the evident relationship which nevertheless exists between the pyloric sphincter and gastric acidity is the problem of measuring the degree of activity of the pylorus, which has been called by Carman [6] the great "X quantity" in roentgenologic investigation of the stomach. Most observers have taken the emptying time of the stomach as a measure of pyloric activity even though factors other than the opening and closing or the "tonus" of the sphincter may be of even greater significance. Certain of them, it is true, may be standardized such as the kind of food, or its bulk or fluidity. Neuromuscular factors, however, such as gastric peristalsis and "gastric tone" as well as the important influence of the amount of food in the duodenum,[7] are usually beyond control. A still further source of confusion has been the use of various "test meals" to evoke a gastric response or, more particularly, acidity in the contents of the stomach. The results are generally of great variability even when produced by simple means. When excited by protein the degree of acidity developed is frequently masked by its combination with the test substance. In any case the acidity measured does not really represent the true gastric response, but, as pointed out in our previous papers, is probably a resul-

5. Serdjukow, A. S.: Diss., St. Petersburg, 1899; cited by Babkin (footnote 3, p. 802). Hedblom, C. A., and Cannon, W. B.: Am. J. M. Sc. **108**:504, 1909. Moritz: Ztschr. f. Biol. **42**:589, 1901.

6. Carman, R. D.: Roentgen Diagnosis of Diseases of Alimentary Tract, ed. 2, Philadelphia, W. B. Saunders Company, 1921, p. 1929.

7. Alvarez, W. C.: The Mechanics of the Digestive Tract, ed. 2, New York, Paul Hoeber, Inc., 1928, p. 178.

tant of two factors, gastric secretion and neutralization, the latter factor being frequently overlooked. Variations are therefore not surprising and make deductions all the more difficult. An interesting review of the entire question of the control of the pylorus can be found in the recent monograph by Alvarez.[7]

Experiments directed toward altering the pylorus itself with subsequent study of gastric acidity have been few. In general, gastric acidity has been found much lower both in human beings and in dogs following various types of pylorectomy.[8] Thompson[9] has recently shown experimentally that this change is greater the more completely the pylorus is removed. He also proved that this reduction is not due to alterations of secretion, for the juice from a Pavlov pouch in such dogs showed a normal acidity. After pyloroplasty in which the sphincter is cut across a similar lowering of gastric acidity has been observed both in human beings[10] and in dogs.[11] Deaver and Burden[12] have recently removed the anterior half of the entire pyloric wall in man for pylorospasm and duodenal ulcer. Reduction of gastric acidity was not observed, although the patients were reported as greatly relieved by the operation. Unfortunately, in all these operative procedures structures other than the sphincter are altered, so that clear inferences are unjustified. The simplest form of pyloric insufficiency, such as may be produced by cutting across the muscle alone, has apparently escaped experimental study, at least from the point of view of its effect on gastric acidity. Strauss[13] removed a triangular piece of the pyloric muscle in dogs and noted a persistent lowering of the emptying time, but reported no observations on gastric acidity. Incision of the hypertrophic pylorus in infants is a frequent operation, but no studies of the contents of the stomach have apparently ever been made in them. It is interesting, however, that a few years ago Zahorsky[14] described a condition (he called it the "Zed reaction") which immediately followed the Rammstedt operation for the relief of pyloric stenosis in infants. The prominent symptom was watery diarrhea in spite of a gain in weight. That this was probably due to the sudden development of intestinal regurgitation is shown by the finding of *Bacillus coli* in the stomach in such cases. That an anacidity also exists is made likely by the fact that clinical cure results from the feeding of acid to these infants. Indeed,

8. Babkin (footnote 3, p. 443).
9. Thompson, H. L.: Proc. Staff Meet., Mayo Clin. **5**:88, 1930.
10. Finney, G. G.: Personal communication to the authors.
11. Olch (footnote 1, third reference).
12. Deaver, J. B., and Burden, V. G.: S. Clin. North America **9**:1003, 1929.
13. Strauss, A. A.: Longitudinal Resection of the Lesser Curvature, J. A. M. A. **82**:1765 (May 31) 1924.
14. Zahorsky, J.: M. Clin. North America **9**:117, 1926.

the use of lactic acid milk is said to have received much impetus from its success in such cases.[15]

METHODS

The behavior of gastric acidity was studied in a special way by means of an "acid test meal." Healthy dogs of from 8 to 12 Kg. were selected, and after an appropriate fast were given 200 cc. of 0.5 per cent hydrochloric acid by gavage; samples were removed every twenty minutes and titrated for "free" and "total" acid. A "neutralization" curve was then plotted which represented, not the gastric response to a stimulus, but the effectiveness and rapidity with which acid, once present in the stomach, is neutralized and discharged into the duodenum. A detailed description of this method and a discussion of its advantages will be found in our previous papers.[16] Normal curves varied but little between dogs of the same size. Nevertheless, two or three tests were often made preparatory to operation.

Operations were carried out with aseptic precautions and under complete ether narcosis. Through a right rectus incision the pylorus was brought up into the wound. With careful use of a sharp scalpel all the circular pyloric fibers were cut by a longitudinal incision across them carried down to the submucosa. It was necessary to be sure that all fibers were severed else regeneration rapidly took place. Perforation, on the other hand, had to be avoided in order to obviate the scarring and narrowing which followed suturing it. A good pout or bulge of the submucosa into the incision attested the completeness of the dissection. Any slight bleeding was usually controlled readily by a hot pack. Only occasionally was a ligature necessary. The raw area was then carefully covered with omentum, which prevented the growth of scar between the cut ends of the muscle and precluded the development of adhesions to surrounding structures. The wound was then closed in layers. Observations on the neutralization of the "acid test meal" were carried out within fourteen days after operation and for varying periods up to ten months. The animals were killed with chloroform and the condition of the pylorus carefully noted. Control experiments consisted of similar incisions over the duodenum and prepyloric antrum and of simple laparotomy.

OBSERVATIONS

In a great many control dogs there was no change in the neutralization curve even after two or more operations, other than cutting of the pylorus, were performed in the same animal. In several early experiments no change or only a transient one was noted even after division of the pyloric sphincter or excision of part of it. In each of these cases it was found at autopsy that pyloric insufficiency had not been achieved. The incision was incomplete, new muscle or fibrous tissue had grown across the incision, or there were firm adhesions between the pyloric scar and liver or the gallbladder. But in eight dogs permanent changes were observed which were considered satisfactory for the experiment. Four died of accidental causes at periods shorter than four months after operation. Four of them lived from four to ten months,

15. Hartmann, A. F.: Personal communication to the authors.
16. Elman (footnote 1, first and second references).

after which observations were discontinued. These experiments will be described in detail. In each case at autopsy a complete pyloric insufficiency was demonstrable by the pouting or bulging of the submucosa through the incision and the absence of adhesions between it and the surrounding organs. (See figs. 2, 3, 6 and 8.)

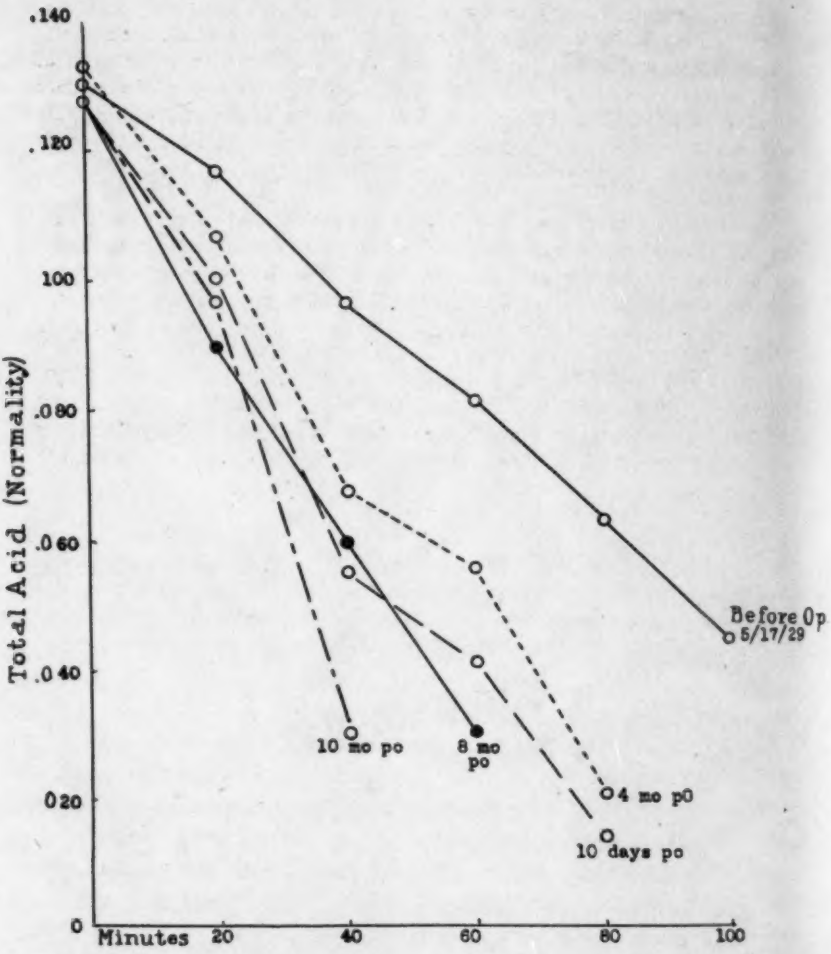


Fig. 1.—Neutralization curves for dog 349, weighing 12 Kg. The dog was killed on March 25, 1930, and showed a definite pouting at the pylorus with no adhesions. Figure 2 represents the gross specimen and figure 3 a section through the pylorus.

The change was apparent soon after operation (the earliest observations were made on the fifth day) and consisted in a more rapid drop in the acidity of the test solution and usually a quicker emptying time.

The observations are represented in the accompanying charts (figs. 1, 4, 5 and 7), which are self-explanatory. The control experiments were negative and will not be mentioned further, since one is represented in dog 161, in which such control observations were made previous to the

Fig. 2.—Photograph of gross specimen from dog 349. The lumen of the specimen was filled with water before fixation. The arrows show the pouting of the submucosa through the pyloric incision.

Fig. 3.—Sketch from a longitudinal section through the area indicated by arrows in figure 2, showing the absence of muscularis (represented by the solid black) over the incised pylorus.

splitting of the pylorus. As will be noted in the protocol and chart of this animal, incisions over the prepyloric antrum and duodenum were without effect; only after the pyloric sphincter was successfully cut did the usual drop in the neutralization curve take place (fig. 4). The

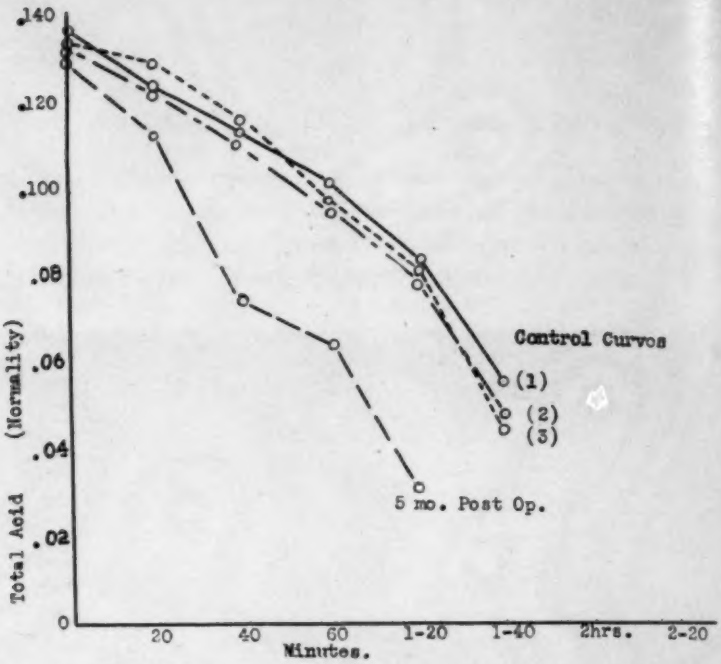


Fig. 4.—Neutralization curves for dog 161, weighing 11 Kg. Control curves (1, 2 and 3) show the absence of any effect of incisions over the prepyloric antrum and duodenum. The curve five months after splitting of the pyloric sphincter is shown below. Autopsy showed a good pout at the site of incision (see protocol in text).

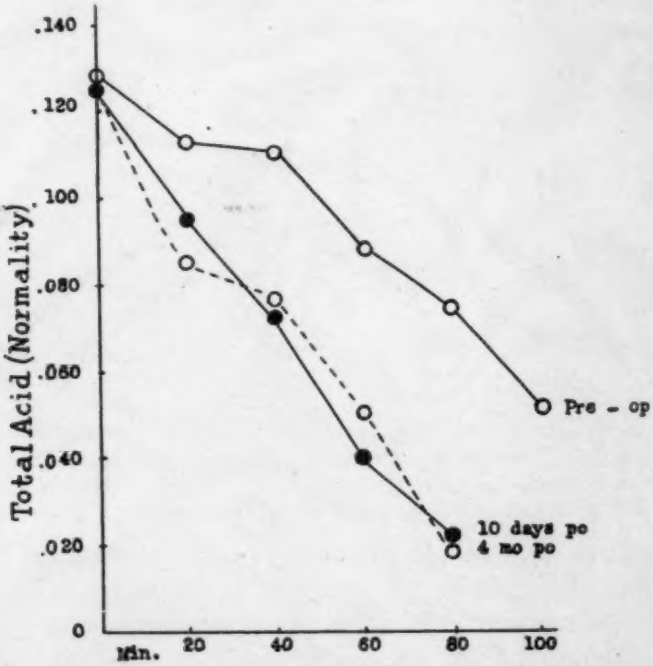


Fig. 5.—Neutralization curves for dog B14, weighing 9 Kg. Accidental death occurred five months after operation. Autopsy showed no adhesions and a good pout of the submucosa through the incision. Figure 6 shows a cross-section through the pylorus.

Fig. 6.—Sketch from a cross-section of the pylorus in dog B14, showing the absence of muscularis (represented by the solid black) over the incised pylorus.

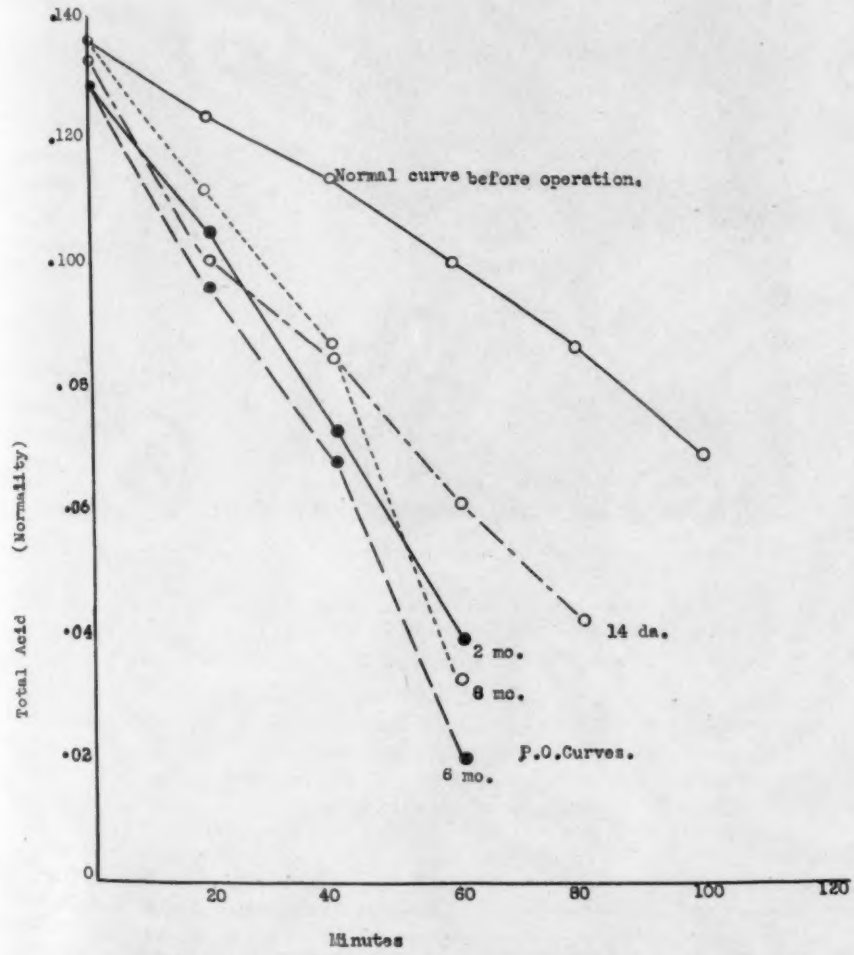


Fig. 7.—Neutralization curves for dog 303, weighing 11 Kg., killed six months after operation because of extensive involvement of the skin with mange. Autopsy showed a good pout and no adhesions. Figure 8 shows the gross specimen cut open.

observations at autopsy in this dog are also of special interest, and a protocol will therefore be given.

Dog 161, a black female, weighed 11 Kg. The neutralization test made before operation showed the usual curve (curve 1, fig. 4). On Feb. 19, 1929, a longitudinal incision about 2 inches (5 cm.) long was made on the anterior surface of the prepyloric antrum from the incisura to the beginning of the pylorus. The submucosa pouted into the opening, which was covered with omentum. One month later another test showed no change (curve 2, fig. 4). At a second operation the prepyloric incision was found intact, not adherent, with no scarring across its edges. An incision was made along the duodenum distal to the pylorus and covered with omentum. Curve 3 in figure 4 shows no change several weeks later. The dog was not observed over the summer months, but on September 25

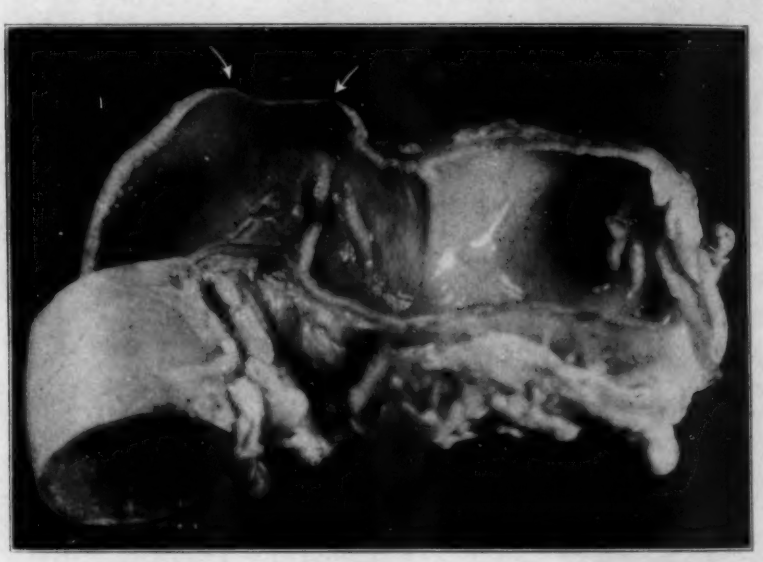


Fig. 8.—Photograph of gross specimen from dog 303. The lumen of the specimen was filled with water before fixation, and then the anterior wall was cut away. The arrows indicate the incised part of the pylorus. Sections of this area show the same picture as represented in figure 3.

showed no alteration in the neutralization curve (not shown in fig. 4). At operation the next day the pyloric sphincter was carefully cut across as described. This time there was a decided drop in the neutralization curve on repeated tests after operation. The curve obtained at five months is represented in figure 4. Shortly afterward the dog showed signs of gastric irritability and vomited; it was found dead on March 16, 1930. Autopsy revealed a good pout through the pyloric incision, with no adhesions around it except to the protecting layer of omentum. The prepyloric and duodenal incisions had both healed with little trace. The pancreas was hard and white and had several areas of fat necrosis in its capsule and a few in the surrounding mesentery. When the duodenum was opened, a small perforating ulcer was found on its posterior wall just distal to the pylorus, which opened into a small cavity full of tangled hair.

COMMENT

The observations herein reported indicate that gastric acidity is more rapidly neutralized and the gastric emptying time somewhat reduced consequent to successful division of the pyloric sphincter, and that this effect persists as long as ten months, or the duration of the observations. It does not seem unfair to infer that the removal or diminution of this barrier renders the stomach more readily accessible to duodenal contents, notably alkaline pancreatic juice, which is thus more easily regurgitated, augments neutralization and makes for a low gastric acidity. If this is true, the theory may be advanced that gastric acidity may be regulated by the pylorus rather than vice versa, i. e., that one may perhaps speak of the pyloric control of gastric acidity.

It is, of course, possible that these observations may be explained in another way. Thus, one may suppose that the acid solution is more rapidly neutralized in these experiments because it is being discharged from the stomach more rapidly, assuming that factors within the stomach are wholly responsible for its neutralization, and there is, thus, much less of the acid to neutralize. From an examination of our data, however, the increased emptying time is not always a prominent feature of the change and, indeed, in some of the experiments did not occur.

More significant, however, is the fact that the existence or at least the importance of these intrinsic gastric factors has not been amply demonstrated. Mucus, for example, was observed in these experiments only in the last samples and often not at all. The secretion by the stomach of a neutral chloride which lowers gastric acidity by dilution is assumed by MacLean and Griffiths [17] on the basis of many special fractional test meals in man. This idea is similar to Pavlov's old assumption of a "Verdünnungssaft," an idea which fell by the wayside because of insufficient support.[3] The most significant facts indicating that intrinsic gastric factors probably play but a minor rôle are that they fail to operate under so many experimental conditions. Thus, it has been shown that neutralization does not take place when the pylorus or pancreatic ducts are tied, is slowed in partial pyloric obstruction, and is absent when the pancreatic juice is drained to the outside.[18]

The present observations would seem to account for the frequent association between anacidity and a patulous pylorus, the latter favoring reflux of pancreatic juice and thus explaining the former. It brings up the question of the cause of anacidity so frequently found in, and often considered essential to, the diagnosis of gastric carcinoma. That this is scarcely due to absence of secretion is shown by the frequent finding of great stretches of normal appearing and staining gastric

17. MacLean, H., and Griffiths, W. J.: J. Physiol. **66**:356, 1928.

18. Elman (footnote 1, first and second references). Babkin (footnote 3).

mucous membrane at autopsy even when large parts of the organ are involved in the new growth. Nor is the finding of anacidity invariable. We have seen several cases recently in which normal acidity was present. In several patients with proved carcinoma of the stomach, too few to draw general conclusions, one of us (R. E.) has obtained very rapid neutralization curves after "acid test meals," which suggests that either a patulous pylorus may account for the anacidity or that the growth acts as a splint to the muscle preventing contraction and thus promoting duodenal regurgitation. The delayed emptying of the stomach frequently noted on roentgen examination of cases of gastric carcinoma does not necessarily preclude this idea, because if the wall of the stomach is splinted by the growth it cannot empty adequately. Recently, Hughson,[19] by "splinting" the pylorus in a special way, was able to show an increase in the healing of experimental ulcers, though unfortunately he made no studies of gastric acidity.

If the pylorus plays an important rôle in regulating gastric acidity, it explains the frequent observations of hyperacidity in cases with dynamic pylorospasm from ulcer or reflex causes, and emphasizes the importance of this structure in the cure of such conditions. It is of interest to note that in a recent paper by Einhorn [20] several patients, poor surgical risks, are reported as greatly relieved from symptoms of duodenal ulcer by stretching of the pylorus without operation. This was done by having the patient swallow a collapsed balloon which was then allowed to pass into the duodenum. The balloon was then sufficiently inflated and pulled back through the pylorus. Analogous to this, perhaps, is the relief often seen following manual dilatation of a spastic sphincter ani both in promoting colonic motility and in the healing of fissures of its mucous membrane. Experiments are now in progress attempting to produce a condition of increased pyloric activity. In one such experiment in which a circular ligature was placed around the pylorus—insufficient to cause obstruction, but presumably enough to prevent full relaxation—a definite delay in neutralization was demonstrable.

The observations on dog 161 (see protocol) deserve special mention, for they illustrate anew the rôle of the pancreatic juice as well as of the pyloric sphincter in protecting the duodenum from the insults of acid gastric juice and have suggestive bearings on the question of the pathogenesis of duodenal ulcer. In a previous paper [21] from this laboratory

19. Hughson, Walter: Relation of the Pylorus to Duration of Experimental Gastric Ulcer, Arch. Surg. **15**:66 (July) 1927.

20. Einhorn, Max: M. J. & Rec. **131**:285, 1930.

21. Elman, Robert, and Hartmann, A. F.: The Cause of Death Following Rapidly the Total Loss of Pancreatic Juice, Arch. Surg. **20**:333 (Feb.) 1930.

the finding of such lesions following persistent drainage of the pancreatic juice to the outside was noted. In this experiment a similar absence of this alkaline secretion occurred by spontaneous disease of the gland. The insufficient sphincter presumably aggravated the condition by allowing acid gastric juice free access to the unprotected duodenum. This suggests the conception of an adequate preparation of gastric contents for reception by the duodenum, which has been convincingly elaborated by Apperly [22] on the basis of his own observations, and which is receiving increasing support. That its failure may have something to do with the genesis of duodenal and even gastrojejunal ulcers is a theory for which considerable evidence exists.

SUMMARY

Experiments are described in which successful division of the pyloric sphincter was achieved and which as a consequence show a persistent lowering of gastric acidity as measured by an augmented neutralization of an "acid test meal." A moderate increase in the emptying time was also observed. Inferences from this and other evidence seem to justify the conception of "the pyloric control of gastric acidity" rather than that of unqualified acid control of the pylorus. Certain clinical implications are discussed.

22. Apperly, F. E.: Brit. J. Exper. Path. **7**:111, 1926.

PYLORIC BLOCK

WITH SPECIAL REFERENCE TO THE MUSCULATURE, MYENTERIC PLEXUS AND LYMPHATIC VESSELS *

BAYARD T. HORTON, M.D.
ROCHESTER, MINN.

MUSCULATURE AND MYENTERIC PLEXUS

One of the interesting facts about the physiology of the gastro-intestinal tract is that peristaltic waves coursing over the stomach seem to stop at the pylorus or a few centimeters above it. Many investigators (Joseph and Meltzer,[1] Wheelon and Thomas,[2] Alvarez and Mahoney,[3] Payne and Poulton [4] and Ivy and Vloedman [5]) have frequently observed tonus waves in the duodenum as the gastric wave approached the pylorus. At times it seems as if the gastric waves actually jump the pyloric barrier and extend down the duodenum as peristaltic rush waves (Alvarez [6]). And yet, the best evidence points to the fact that the duodenal waves originate in the first part of the duodenum and are not propagated gastric waves which have jumped the pyloric barrier (Cole [7] and Alvarez). Why do not the gastric waves go on down the bowel, and why are they blocked at the pylorus? It has been suggested that the block may be due to the anatomic peculiarities in this region or to

* Submitted for publication, March 17, 1930.

* From the Division of Medicine, the Mayo Clinic.

* Work done in the Section on Pathologic Anatomy, the Mayo Clinic. In this paper is reported the greater part of the work for which the John Horsley Memorial Prize for 1929 was awarded by the University of Virginia. The remainder appeared in the American Journal of Anatomy (**61**:197, 1928).

1. Joseph, L. R., and Meltzer, S. G.: Inhibition of the Duodenum Coincident with the Movements of the Pyloric Part of the Stomach, Am. J. Physiol. **27**:31 (Feb.) 1911.

2. Wheelon, H., and Thomas, J. L.: Observations on the Mobility of the Duodenum and the Relation of Duodenal Activity to that of the Pars Pylorica, Am. J. Physiol. **59**:72 (Feb.) 1922.

3. Alvarez, W. C., and Mahoney, Lucille J.: The Relations Between Gastric and Duodenal Peristalsis, Am. J. Physiol. **64**:371 (April) 1923.

4. Payne, W. W., and Poulton, E. P.: Visceral Pain in the Upper Alimentary Tract, Quart. J. Med. **17**:53 (Oct.) 1923.

5. Ivy, A. C., and Vloedman, D. A.: The Small Intestine in Hunger, Am. J. Physiol. **72**:99 (March) 1925.

6. Alvarez, W. C.: The Mechanics of the Digestive Tract, ed. 2, New York, Paul B. Hoeber, Inc., 1928, pp. 447.

7. Cole, L. G.: Motor Phenomena of the Stomach, Pylorus and Cap Observed Roentgenographically, Am. J. Physiol. **42**:618 (March) 1917.

the physiologic differences that exist between the muscle in the pyloric antrum and that in the duodenum. Of the many descriptions of the anatomic structure of the stomach in man, there are relatively few concerning the block at the pylorus and the relationship of the circular and longitudinal fibers in this area to those of the duodenum, and there are no references, so far as I am aware, regarding the continuity of the myenteric plexus. In Morris' "Human Anatomy" [8] (seventh edition) it is stated that the circular fibers of the stomach are continuous with the circular fibers of the duodenum, while in Gray's "Anatomy of the Human Body" [9] (twentieth edition) it is stated that the circular fibers of the stomach are not continuous with those of the duodenum. These volumes contain little regarding the other structures in this area. Furthermore, practically nothing is known about the generic and individual variations in this area, either in the lower animals or in man. And yet, "probably no portion of the digestive tube bears so close a relation to all diseases of the stomach and duodenum, as does the pylorus itself. And there is probably no field in the whole subject of medicine about which we have so little absolute knowledge as that of the neurology of the gastro-intestinal tract" (Hughson [10]). Alvarez and Mahoney (1923) emphasized the importance of additional research in this field.

This study was primarily undertaken with the hope of determining the percentage of circular and longitudinal fibers in the pars pylorica that are continuous with the circular and longitudinal fibers of the duodenum (table), and also to determine, if possible, some of the individual variations that occur in this region. The results, with a review of the literature, have been published (Horton [11]). Therefore, in this paper I shall point out only one possibility that has to do distinctly with the musculature, which was not included in the previous paper. Hypertrophic pyloric stenosis is occasionally observed in the new-born infant and may well be explained by the data represented in figures 1 and 2. Figure 1 represents a section through the pylorus of a male fetus of 6½ months, and figure 2 represents a section through the pylorus of a full term male fetus. The ratio of the thickness of the muscle wall to the lumen may be noted in the two figures. Persistence of the thickened muscle in figure 1 may explain the occurrence of

8. Morris, Henry: Human Anatomy, ed. 7, Philadelphia, P. Blakiston's Son & Company, 1923, pp. 1507.

9. Gray, Henry: Anatomy of the Human Body, ed. 20, Philadelphia, Lea & Febiger, 1918, p. 1165.

10. Hughson, Walter: Reflex Spasm of the Pylorus and its Relation to Diseases of the Digestive Organs, Arch. Surg. **11**:136 (July) 1925.

11. Horton, B. T.: Pyloric Musculature with Special Reference to Pyloric Block, Am. J. Anat. **61**:197 (May) 1928.

Micrometer Measurements of Microscopic Sections of Pylorus, Showing Percentage of Circular and Longitudinal Muscle Fibers Crossing from Stomach to Duodenum

Case	Age, Years	Sex	Sections Measured	Stain		Continuity of Musculature, per Cent	
				Hematoxylin and Eosin	Van Gieson	Circular	Longitudinal
1	20 days	F	10	..	10	....	13.0
2	28 days	F	1,210*	..	1,210	0.12	21.4
3	4 months	F	126	..	126	....	10.8
4	6 months	M	150	..	150	....	53.0
5	8 months	M	150	15	135	....	25.0
6	11 months	M	16	8	8	....	56.0
7	1	M	445†	..	445	....	24.0
8	2	M	79	..	79	....	61.0
9	2½	F	12	..	12	....	....
10	4	F	20	..	20	....	26.4
11	4	F	46	..	46	....	45.1
12	16	F	12	6	6	....	4.0
13	17	M	10	5	5	....	43.5
14	19	M	11	4	7	....	30.0
15	19	F	4	..	4	....	35.0
16	21	F	14	5	9	....	11.5
17	21	F	10	5	5	....	30.0
18	22	M	8	4	4	....	7.5
19	23	F	12	4	8	....	28.0
20	23	M	4	..	4	....	41.7
21	26	F	11	5	6	....	40.0
22	29	M	15	7	8	....	6.9
23	32	M	13	6	7	....	42.5
24	32	M	10	5	5	....	40.0
25	34	F	4	..	4	....	10.5
26	35	M	17	8	9	....	21.0
27	36	M	12	4	8	....	20.0
28	36	F	10	5	5	....	9.9
29	37	F	13	6	7	....	22.5
30	39	M	10	5	5	....	46.5
31	40	M	10	5	5	....	66.0
32	40	F	14	7	7	....	18.8
33	41	M	11	5	6	....	18 0
34	42	F	9	5	4	....	8.6
35	42	F	19	8	11	....	17.0
36	42	M	13	5	8	....	17.9
37	43	M	13	7	6	....	8.6
38	43	F	117	9	108	...	47.0
39	43	F	8	4	4	....	5.0
40	43	F	13	7	6	....	10.0
41	43	F	5	..	5	....	45.0
42	44	M	9	5	4	....	37.0
43	45	F	8	4	4	....	43.0
44	45	F	13	5	8	....	24.0
45	45	M	12	6	6	....	37.0
46	45	M	12	5	7	....	23.5
47	46	F	10	6	4	....	48.6
48	47	M	12	6	6	....	10.0
49	48	F	16	8	8	....	52.0
50	48	F	12	6	6	....	17.2
51	48	F	10	6	4	....	16.2
52	49	M	14	7	7	0.5	12 3
53	50	F	8	4	4	....	7.5
54	51	F	15	6	9	....	2.6
55	51	F	10	5	5	....	14.2
56	53	F	11	5	6	....	25.7
57	53	M	12	6	6	....	22.4
58	54	M	13	7	6	....	26.2
59	55	M	17	8	9	....	16.4
60	55	M	10	5	5	2.0	33.0
61	55	F	8	4	4	....	23.5
62	55	F	9	5	4	....	19.6
63	56	F	11	6	5	....	12.0
64	59	M	10	4	6	....	40.0
65	62	F	11	4	7	....	21.0
66	62	M	12	6	6	....	5.8
67	62	F	11	5	6	....	4.5
68	64	M	8	4	4	....	25.0
69	65	M	11	6	5	....	13.0
70	67	M	10	5	5	....	7.9
71	67	F	11	5	6	....	7.2
72	67	F	12	6	6	....	26.8
73	69	F	10	5	5	....	3.9
74	69	M	10	5	5	....	24.0
75	70	M	22	9	13	....	15.2
76	70	F	13	7	6	....	25.5
77	71	M	5	..	5	....	22.8
78	72	M	8	4	4	....	4.6
79	73	M	12	6	6	....	10.2
80	74	M	19	8	11	....	12.9
81	74	M	14	7	7	....	11.0
82	74	M	9	5	4	....	63.0
83	75	M	4	..	4	....	22.0
84	76	M	4	..	4	....	41.0

* Each of 1,210 sections in this series was measured.
† Of the 1,335 sections in this series, every third section was measured.

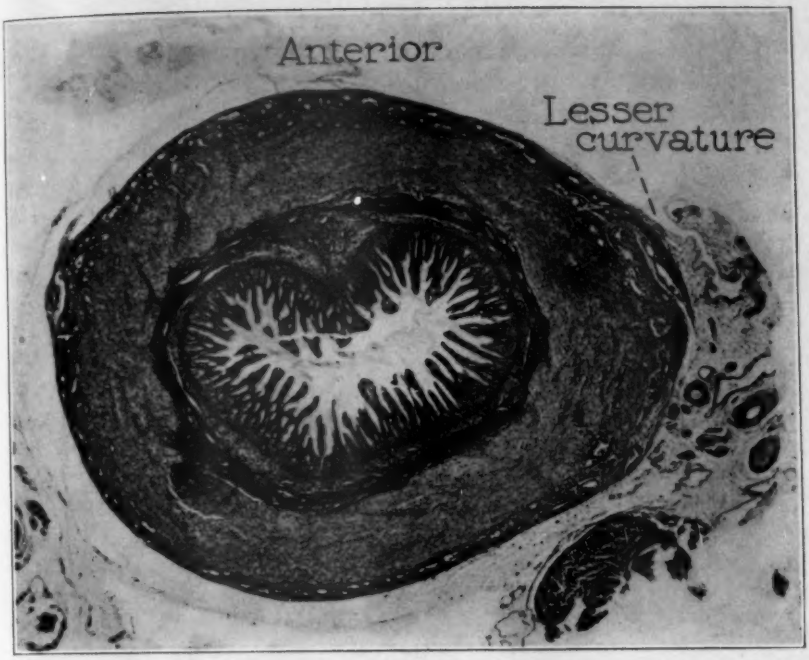


Fig. 1.—Cross-section of the pylorus in a male fetus of 6½ months (× 18).

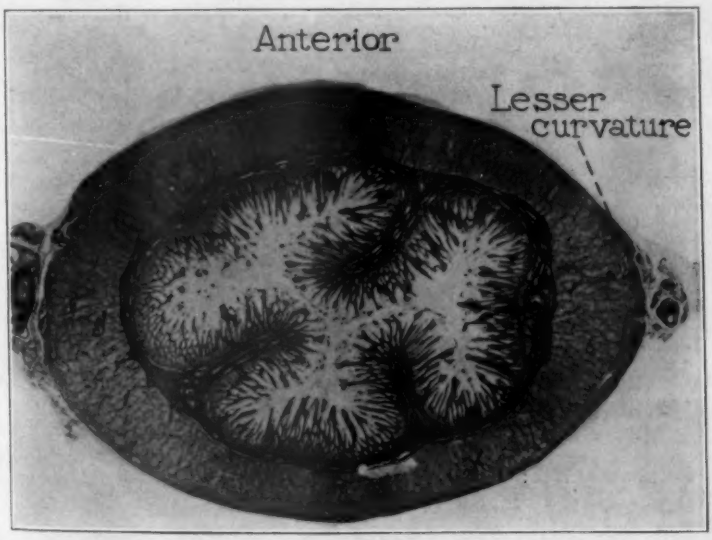


Fig. 2.—Cross-section of the pylorus in a male fetus at full term (× 10).

hypertrophic pyloric stenosis at birth. From a study of embryonic and fetal stomachs, a relatively thick pylorus at the fifth to sixth month of development is a usual observation.

As the work developed, I soon realized that other structures at the pylorus would be just as interesting to the investigator, and as a result, the problem was broadened to include a study of the myenteric plexus and the lymphatic vessels. Williams,[12] working in the same laboratory with me, has since demonstrated an almost complete block in the anastomosis of intramural arteries across the pyloric sphincter.

Review of the Literature.—Auerbach,[13] in 1862, first described the nerve plexus that bears his name. Since that time many investigators have contributed to the knowledge of the subject (Cajal,[14] Kölliker,[15] Dogiel,[16] Müller[17] and Kuntz[18]), but there are no references in the literature, so far as I am aware, regarding the continuity of the myenteric plexus (Auerbach's plexus) from the stomach to the duodenum. Dr. Kuntz,[19] professor of anatomy at St. Louis University, stated that he knew of no work on the subject, and yet he has been interested in the autonomic nervous system for the last twenty-one years and has contributed many excellent articles to the literature. Other anatomists (Dr. R. E. Scammon,[20] of the University of Minnesota, and Dr. H. A. Harris,[21] at the University College of London) have made similar statements. Hill,[22] in a recent article, gave the best review of the literature on the myenteric plexus, but made no statement regarding

12. Williams, T. B.: Vascular Studies of the Pylorus, Anat. Rec. **38**:273 (May) 1928.

13. Auerbach, L., quoted by Oppel, Albert: Lehrbuch der vergleichenden mikroskopischen Anatomie der Wirbeltiere, Jena, Gustav Fischer, 1896, vol. 1, p. 27.

14. Ramón Cajal, S., quoted by Kuntz, Albert: J. Comp. Neurol. **23**:173 (June) 1913; quoted by Hill, C. J.: Philos. Tr., London **215**:355 (Jan.) 1927.

15. Kölliker, Albert: Ueber die feinere Anatomie und die physiologische Bedeutung des sympathischen Nervensystem, Vienna, Wilhelm Braumüller, 1894, p. 24.

16. Dogiel, A. S., quoted by Kuntz, Albert: J. Comp. Neurol. **23**:173 (June) 1913; quoted by Hill, C. J.: Philos. Tr., London **215**:355 (Jan.) 1927.

17. Müller, L. R., quoted by Kuntz, Albert: J. Comp. Neurol. **23**:173 (June) 1913.

18. Kuntz, Albert: On the Innervation of the Digestive Tube, J. Comp. Neurol. **23**:173 (June) 1913.

19. Kuntz, Albert: Personal communication to the author.

20. Scammon, R. E.: Personal communication to the author.

21. Harris, H. A.: Personal communication to the author.

22. Hill, Catherine J.: A Contribution to Our Knowledge of the Enteric Plexus, Philos. Tr., London **215**:355 (Jan.) 1927.

this plexus at the pylorus. Latarjet,[23] Brandt[24] and McCrea[25] stated that the vagal fibers extend up to the pylorus, but do not cross it. The literature regarding the innervation of the pyloric sphincter is confusing. Many workers contend that vagal influence is for contraction and sympathetic influence is for relaxation, while others maintain the reverse of this hypothesis. The best evidence seems to support the former view.

Methods and Material Studied.—The material used in this study, as set forth in a previous paper (Horton,[11]), was obtained from postmortem examinations at the Mayo Clinic.

For the study of the myenteric plexus, blocks of tissue were taken from six normal stomachs at points 1, 2, 3 and 4, as shown in figure 3. They were obtained from subjects aged less than 1 year. Serial sections 10 microns thick were made from each block. They were cut parallel with the long axes of the pyloric canal and extended from 5 to 8 mm. into the duodenum. A modification of the Orlandi stain, which Kernohan[26] has described, and the van Gieson stain were used to

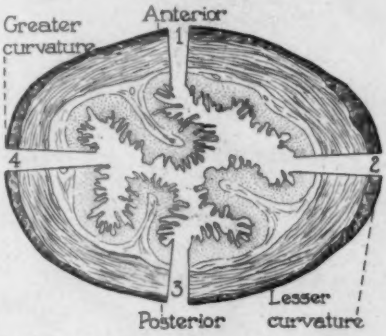


Fig. 3.—Cross-section of the pyloric canal in a full term fetus about 1 cm. above the pyloric sphincter.

bring out the myenteric plexus. By means of a projectoscope, the microscopic picture was projected on a screen, and areas of nerve tissue, together with an outline of the mucosa and musculature, were traced on paper and transferred to thin glass plates, Enamel paint and india ink were used to make the drawings on the glass plates. A definite color was used to represent each structure transferred to the plates, and this color scheme was carried out in all of the reconstructions. From twenty-five to sixty microscopic sections from a given serial, taken in consecutive order, were traced on glass plates, and the plates stacked in consecutive order. With a strong light behind the stack of plates, an excellent picture is obtained. When the glass plates are accurately superimposed in consecutive order, the various elements of the myenteric plexus form a continuous,

23. Latarjet, A., quoted by Hughson, Walter: Arch. Surg. **11**:136 (July) 1925.

24. Brandt, W.: Die Innervation des Magens, Ztschr. f. ang. Anat. **5**:302, 1920.

25. McCrea, E. D.: The Abdominal Distribution of the Vagus, J. Anat. **59**:18, 1924.

26. Kernohan, J. W.: Adaption of Bielschowsky's Silver Impregnation Method for Material Imbedded in Paraffin or Celloidin, to be published.

although winding, chain from the stomach to the duodenum. This method of using glass plates has not been used at the Mayo Clinic before, and at the time I devised the method I had not found a reference to it in the literature.

Results.—The myenteric plexus is continuous from the stomach to the duodenum, as shown in figures 4, 5, 6 and 7. This was true in all of the cases studied. Reconstructions from various segments of the pyloric ring showed variations in the appearance of the ganglionic chain, but these variations seemed to be due to the irregularity in arrangement of the muscle fibers in this area. The ganglions of the myenteric plexus are irregular aggregates of neurons interposed between the circular and longitudinal muscle coats and are connected with each

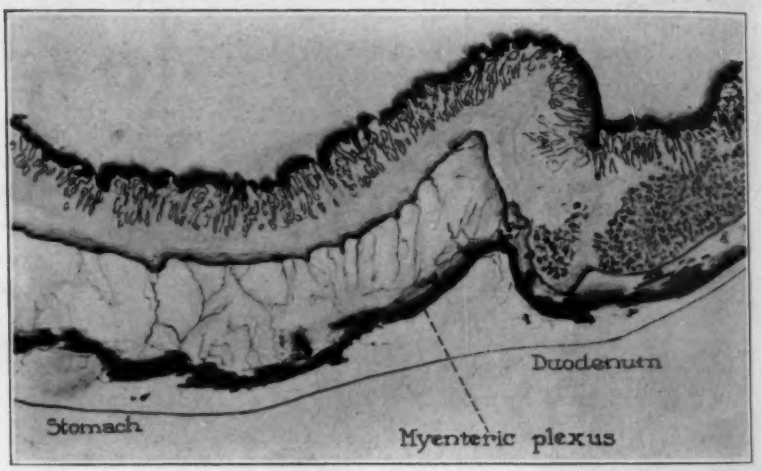


Fig. 4.—Reconstruction of the myenteric plexus, showing the continuity from the stomach to the duodenum. This is a drawing of a glass model that was made from twenty-nine serial sections. It represents a longitudinal block through point 4 in figure 3. The subject was a boy, aged 8 months.

other by bundles or bands of nonmedullated nerve fibers. The ganglions of the submucous plexus are much smaller collections of neurons, connected in a similar manner, although in many sections it is difficult, and frequently impossible, to trace the connections. The connections between the two plexuses are frequently easy to trace, and it would seem from the histologic structure that the submucous plexus represents a subdivision of the larger myenteric plexus. Fine fibrils from the submucous plexus can be seen to terminate on or adjacent to the epithelial cells lining the digestive tube, while the fibrils from the myenteric plexus can frequently be seen to terminate on muscle cells.

Fig. 5.—Longitudinal section through the pylorus, showing the myenteric plexus between the circular and the longitudinal muscle, in the duodenopyloric juncture in a female subject, aged 4 weeks (× 25).

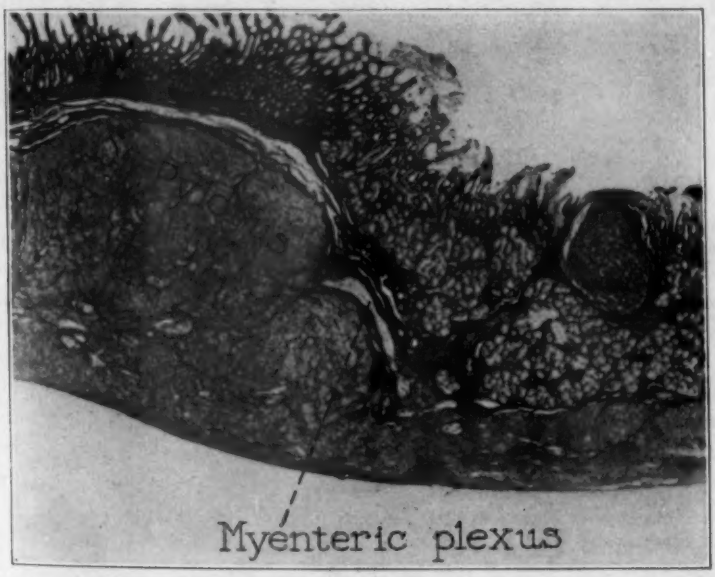


Fig. 6.—Longitudinal section through the pylorus, showing the myenteric plexus in the submucosa at the duodenopyloric juncture in a male subject, aged 1 year (× 22).

The myenteric plexus was normally found between the circular and the longitudinal muscle coats (fig. 5), but in one specimen (figs. 6 and 7) the continuity of the myenteric plexus from the stomach to the duodenum was by way of the submucosa. In this specimen, at the duodenopyloric juncture, the myenteric plexus (Auerbach's plexus) occupied the position normally occupied by the submucous plexus (Meissner's plexus). This is probably a fairly normal occurrence in this area, and perhaps definite significance cannot be attached to the observation. Reconstructions of Meissner's plexus have not been made.

Comment.—It is apparent from the results of this study that there is an almost complete separation between the circular muscle of the

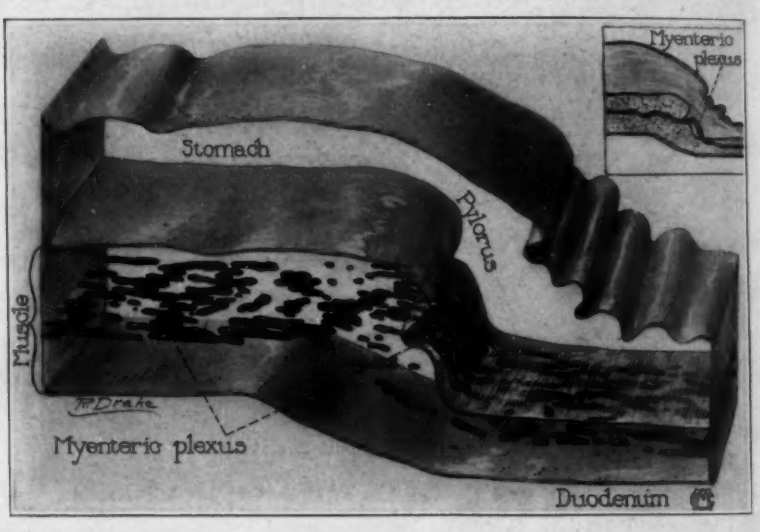


Fig. 7.—Reconstruction of the myenteric plexus illustrated in figure 6, showing the continuity from the stomach to the duodenum by way of the submucosa. The drawings are of a glass model, which was made from sixty serial sections. It represents a longitudinal block through point 2, figure 3. The insert is the view one obtains when looking down through the model from above. The subject was a boy, aged 1 year.

stomach and the duodenum, an interruption of continuity with physiologic significance, as Cannon [27] expressed it, and partial block of the gastric longitudinal fibers. The interruption of the circular muscle at the duodenopyloric juncture undoubtedly accounts for the block in peristaltic waves at the pylorus. The changes in tonus that are frequently observed in the duodenum, with the approach of gastric waves, are probably due to the spread of some influence along the myenteric plexus,

27. Cannon, W. B.: The Mechanical Factors of Digestion, London, E. Arnold, 1911, p. 227.

or along the narrow bridges of muscle connecting the stomach and duodenum, or perhaps along both routes. If the gastric waves were not blocked at the pylorus, but traveled on down the duodenum, even for a short distance, duodenal ulcer would probably become much less common than at present.

As has already been written (Horton [11]), in the distal portion of the pyloric canal, where most of the longitudinal fibers dip into the circular muscle (to form the dilator muscle of the pylorus), it would certainly seem, from the anatomic arrangement of these fibers, that they must act as a dilator of the pylorus. The marked hypertrophy of these fibers, unassociated with hypertrophy of the circular fibers, which I have observed in annular carcinoma of the pyloric canal with partial obstruction to the pyloric outlet tends to substantiate this view.

LYMPHATIC VESSELS OF THE STOMACH WITH SPECIAL REFERENCE TO PYLORIC BLOCK

Carcinoma of the stomach rarely invades the duodenum. It apparently spreads easily in all directions in the walls of the stomach and often extends to the pyloric ring, but it seems to stop there abruptly. Even in advanced cases, the duodenum may remain free. It is well known that carcinoma usually spreads by direct extension or by way of the lymphatic system. Is there a barrier at the pylorus to the spread of carcinoma? If so, what is the nature of this barrier? Several theories have been advanced in explanation of the immunity of the duodenum. It has been attributed to scarcity of lymphatic vessels between the two organs, to the upward flow of lymph from the duodenum to the stomach, to the alkalinity of the duodenum and to the obliteration of tissue spaces by spasmodic contraction of the pyloric sphincter so as to form a mechanical obstruction to the advance of the carcinoma. I shall consider here the lymphatic drainage of the stomach, the relationship between the lymphatic vessels of the stomach and those of the duodenum and their bearing on the problem.

Review of the Literature.—Excellent historical reviews of the lymphatic system are given by Todd,[28] Cruveilhier,[29] Hewson [30] and Poirier, Cunéo and Delamere.[31] According to the latter authors, Herophilus

28. Todd, R. B.: The Cyclopedia of Anatomy and Physiology, London, Longman, Brown, Green, Longmans and Roberts, 1839-1847, vol. 3, p. 205.

29. Cruveilhier, Jean: The Anatomy of the Human Body, New York, Harper & Brothers, 1844, p. 907.

30. Hewson, William: A Description of the Lymphatic System, London, The Sydenham Society, 1846, p. 119.

31. Poirier, P.; Cunéo, B., and Delamere, Gabriel: The Lymphatics, London, Constable & Company, 1913, p. 301.

(300 B. C.) and Herasistratus (280 B. C.) should be accorded the honor of discovering the chyliferous vessels. But Todd, Cruveilhier and Hewson [32] did not mention any of the writers before Galen, and Todd and Cruveilhier gave Eustachius (1453), who described the thoracic duct in the horse, the honor of discovering the lymphatic system. Sixty-nine years later, Gaspard Asellius (1622), while seeking another object, discovered, on the mesentery of a dog, certain vessels that were carrying a milk-like fluid; he called these vessels lacteals. He died in 1626, without ever seeing the lacteals in man. Pecquet (1641) discovered the receptaculum chyli and showed that the lacteals entered the thoracic duct, and not the liver, as Asellius and his contemporaries believed. Rudbeck (1651) described the lymphatics of the liver, the pancreas, the lungs and the pelvis and concluded from his researches that the "serous vessels" existed throughout the organism and formed a special system. Bartholin, in Denmark, and Jolyffe, in England (about 1652), confirmed Rudbeck's attempt at generalization, and the "serous system" became the lymphatic system. In 1654, the function of absorption was ascribed to this system by Glisson and Hoffmann. After this period Nuck added to the knowledge of this system by injection of the lymphatic glands, Ruysch by his description of the valves of the lymphatic vessels and Meckel by his accurate account of the whole system. Other workers (Albinus, Hunter, Monro, Hewson, Cruikshank and Mascagni) added various details concerning the system. Several years later, Lippi (1822) and Lauth (1824) discovered the existence of peripheral lymphatic venous communications. In 1847, Sappey [33] began his researches, which he continued until the publication of his atlas in 1876. Following Sappey, the chief work on the lymphatics of the stomach has been done by Most (1899), Cunéo (1900), Cunéo and Delamere (1900), Pólya and von Navratil [34] and Jamieson and Dobson.[35] Very little work has apparently been done on the lymphatics of the stomach during the last twenty years. In fact, I have looked through all the volumes of the *Quarterly Cumulative Index Medicus* twice, without finding a single reference dealing with the injection of lymphatics of the stomach. Most textbooks on anatomy state that there are two main areas of lymphatic drainage in the stomach, the one along the lesser curvature and the other

---

32. Hewson added in a footnote that the lacteals had been seen in kids by Erasistratus, who called them arteries. Hewson really gave Asellius the main credit for the discovery of the lymphatic system.

33. Sappey, C.: Cited by Poirier, Cunéo and Delamere (footnote 31).

34. Pólya, Eugen, and von Navratil, Desider: Untersuchung über die Lymphbahnen des Wurmfortsatzes und des Magens, Deutsche Ztschr. f. Chir. **69**:421 (Aug.) 1903.

35. Jamieson, J. K., and Dobson, J. F.: Lectures on the Lymphatic System of the Stomach, Lancet **1**:1061, 1907.

along the greater curvature. The latter is usually divided into two groups, one draining toward the subpyloric group of lymph nodes and the other to the splenic lymph nodes. A few (Gray's anatomy and Cunningham's anatomy) mention four drainage areas, quoting the work of Jamieson and Dobson (1907). Poirier, Cunéo and Delamere (1913) in "The Lymphatics" (page 199), which is the outstanding book on the lymphatic system, stated: "In the stomach there are three distinct lymphatic territories. . . . These territories correspond to the three groups of collecting trunks which we have described." They did not mention the work of Jamieson and Dobson.

The literature dealing with the lymphatics at the pylorus may be summarized as follows: All of the observers stated that there is no continuity between the subserous lymphatic system of the stomach and duodenum, except Sappey, who stated that the subserous lymphatics are directly continuous between the stomach and the duodenum, and Jamieson and Dobson, who found evidence of continuity in one specimen of thirty. All of the outstanding workers in this field (Sappey, Most, Poirier, Cunéo and Delamere, Pólya and Navratil, and Jamieson and Dobson) stated that the submucous lymphatics of the stomach are directly continuous with those of the duodenum, although certain observers (Poirier and Cunéo, Jamieson and Dobson) added that these lymphatic vessels are not highly developed.

Material and Methods.—The material used in this investigation was obtained from necropsies at the Mayo Clinic. Only normal specimens were used. The youngest subject was a fetus aged 7 months, and the oldest a man aged 66. Most of the specimens were obtained from very young subjects. The stomachs were obtained between one and three hours after death; either injections were made while they were in situ, or the stomach and adjacent organs were removed en masse and injections were then made into the stomach while it was immersed in warm water. The standard apparatus for injection work in the Section on Pathologic Anatomy was used. Constant pressure can be maintained over any period of time.

A modification of Gerota's method was employed. India ink and colored gelatin [36] were used as injection mediums. The gelatin mixture, in the liquid state, was essentially of the same consistence as the india ink. It was kept this way by means of a warm water bath. It is an excellent injection medium, for the gelatin hardens when the specimen into which injections are made is placed in a fixative of formaldehyde. Better microscopic sections can be made from such a specimen than from specimens in which india ink alone is used for injection. In all, injections were made into thirty-five specimens. Injections were made into fifteen of these specimens under pressure ranging from 20 to 60 mm. of mercury and into twenty specimens under pressure varying from 180 to 460 mm. of mercury. The needle was invariably inserted into the submucosa of the stomach and was pushed on until it was between 1.5 and 5 cm. from the pyloric sphincter. The injection mass was then allowed to flow into the submucosa. Leakage was not encountered during the time of injection. In ten specimens multiple punctures

36. Gelatin 45 Gm., india ink 60 cc., water sufficient to make 500 cc.

were made in the submucosa, both in the anterior and in the posterior surfaces of the stomach. Injections were made into these specimens under relatively low pressure, from 20 to 60 mm. of mercury. Only a small area of lymph vessels was filled from each puncture. By this method injections were made into the entire collecting system of the lymph vessels. In five specimens injections were made into the submucosa of the doudenum with the point of the needle just distal to the pyloric sphincter. Carmine-colored gelatin was the medium used for the duodenal injections. An average of six microscopic sections through the duodenopyloric juncture, parallel with the long axis of the pyloric canal, was made from each specimen. A detailed study was made of the lymphatics in this area. The carcinomas of the stomach used in this study were also obtained from the necropsy service at the Mayo Clinic.

Results.—In all of the specimens continuity was not evident between the submucous lymphatics of the stomach and the duodenum (figs. 8,

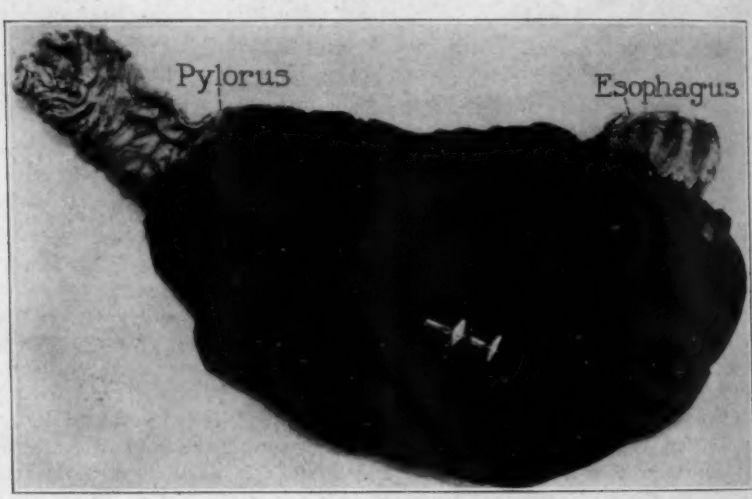


Fig. 8.—Submucosa of the stomach from a female subject, aged 47 years, into which injections of india ink were made under a pressure of 300 mm. of mercury. The needle with which the injection was made is still in place, with the point of the needle in the submucosa 6.5 cm. proximal to the pyloric sphincter. The injection mass has been stopped abruptly at the pylorus.

9, 10 and 11). Complete continuity of the lymphatic network was evident in the submucosa of the stomach. A few of the specimens showed direct continuity between the subserous lymphatics of the stomach and duodenum. This was observed only on the posterior aspect of the pylorus. The specimens varied markedly in the ease with which injections were made into the submucosa. In one specimen (fig. 12) the injection into the submucosa was easy. With the point of the needle in the submucosa 4 cm. proximal to the pyloric sphincter, the ink flowed in freely under a pressure of 180 mm. of mercury, and the entire

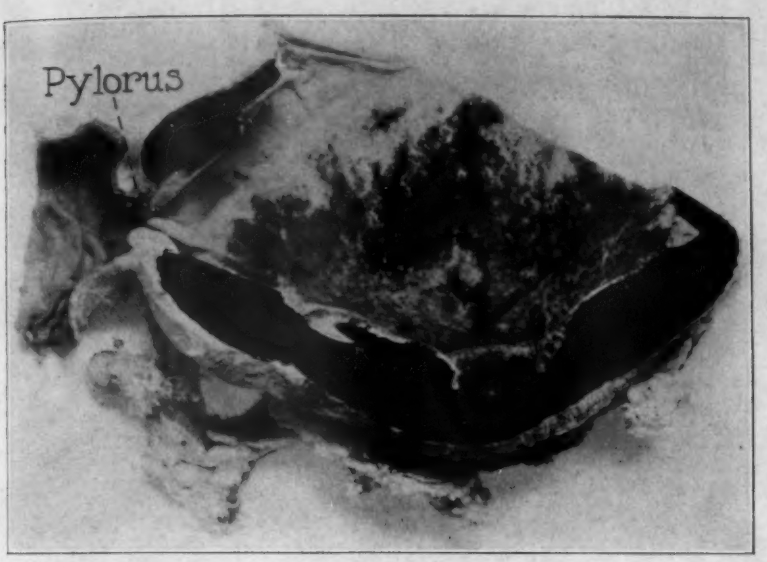


Fig. 9.—Submucosa of the stomach from a male subject, aged 27 years, into which injections of a mixture of india ink and gelatin were made under 20 mm. of pressure with the point of the needle in the submucosa, 2.5 cm. proximal to the pyloric sphincter. The wall of the stomach is infiltrated with the mass that has been blocked at the pylorus.

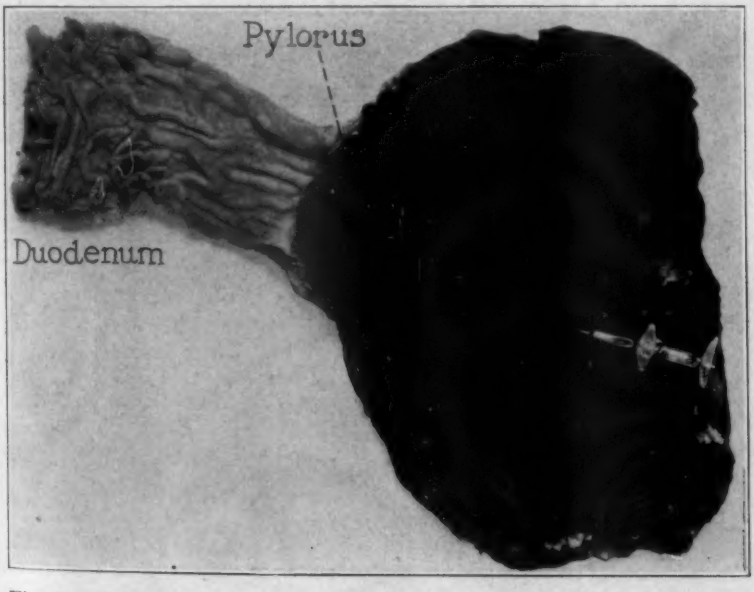


Fig. 10.—Submucosa of the stomach from a female subject, aged 57 years, into which injections of a mixture of india ink and gelatin were made under 460 mm. of pressure, with the point of the needle in the submucosa 3 cm. proximal to the pyloric sphincter. The injection mass has been stopped abruptly at the pylorus. The injection was carried out for a period of two and one-half hours.

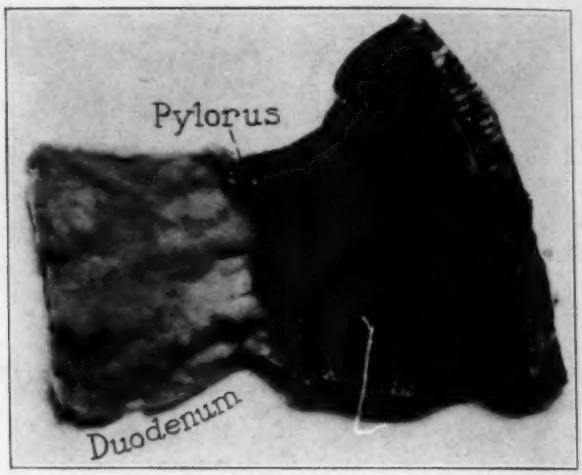


Fig. 11.—Submucosa of the stomach from a male subject, aged 11 months, into which injections of a mixture of india ink and gelatin were made under 280 mm. of pressure, with the point of the needle in the submucosa 2 cm. proximal to the pyloric sphincter. This pressure was maintained for thirty minutes after the injection mass reached the pylorus. Only the pars pylorica received the injection, as a clamp was applied across the middle third of the stomach. The mass has been blocked at the pylorus.

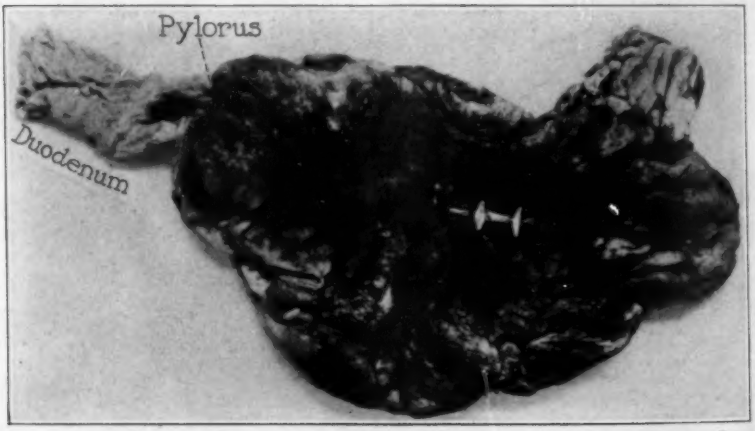


Fig. 12.—Submucosa of the stomach from a male subject, aged 66 years, into which injections of india ink were made under 180 mm. of pressure, with the point of the injection needle in the submucosa 4 cm. proximal to the pyloric sphincter. Slight extravasation of ink into the duodenum has taken place.

submucosa was injected within fifteen minutes. After the stomach was well injected, the submucosa at the pyloric sphincter became slowly but markedly distended and remained so for eight minutes; then the ink slowly extravasated into the submucosa of the duodenum, on the posterior aspect, for a distance of 1 cm. In many specimens into which injections were made in exactly the same manner, even under pressure as high as from 300 to 460 mm. of mercury, the medium stopped abruptly at the pylorus (figs. 8 and 10). After the submucosa at the sphincter had become markedly distended, the pressure was maintained at 460 mm. for thirty minutes, or longer, without any extravasation of ink into the duodenum. In one specimen (fig. 10) with the point of the needle in the submucosa 3 cm. proximal to the pyloric sphincter, after the submucosa had become distended at the pylorus, a clamp was applied across the stomach at its middle portion, proximal to the insertion of the needle, so that the entire pressure of from 420 to 460 mm. of mercury was applied to the pylorus for a period of twenty minutes, but there was absolutely no leakage of ink across the pyloric sphincter into the duodenum. A similar procedure was followed with a child's stomach (fig. 11) under a pressure of 280 mm. of mercury, with similar results. In all of the specimens into which injections were made under high pressure, the stomach was first opened by incision along the anterior surface, midway between the greater and lesser curvatures, the incision extending well down into the duodenum. The state of tonus of the pyloric sphincter was not a factor in these cases, for the pylorus was cut through on the anterior aspect before the injection was started, and the cut margins were either sutured with heavy thread or stomach clamps were applied along the cut margins so as to prevent leakage of the injection medium.

In the majority of specimens it was observed, at the time of injection, that the ink flowed more readily at right angles to the long axis of the stomach. It approached the greater and lesser curvatures, the cardia and the pylorus with decreasing velocity in the order named. In several specimens, by actual measurement, it traveled an average of 12 cm. toward the cardia while flowing 2 cm. toward the pyloric sphincter, even though the current of the injection mass was directed toward the sphincter. In all of the specimens the injection mass flowed up to the pyloric sphincter and stopped abruptly. In some specimens, the submucosa was so distended that it was overhanging the pylorus and projecting into the duodenum; in one specimen the wall of the stomach just proximal to the sphincter was 5 cm. thick, whereas it was 2 mm. thick prior to the injection. Injections were also made into the submucosa of the duodenum in five specimens, with the point of the

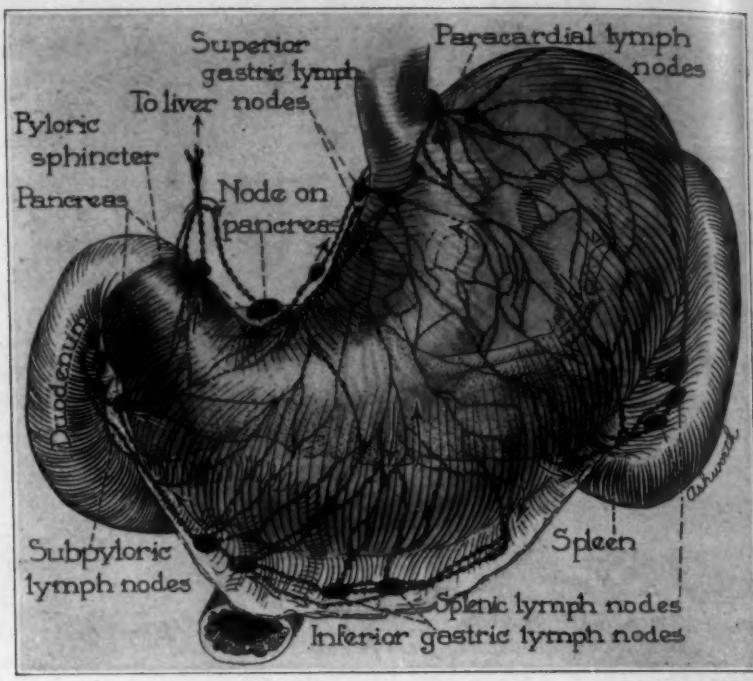


Fig. 13.—Lymphatic drainage of the stomach (anterior surface), as determined by injections into thirty-five specimens. The arrows indicate the lines of drainage. There are four distinct areas of drainage.

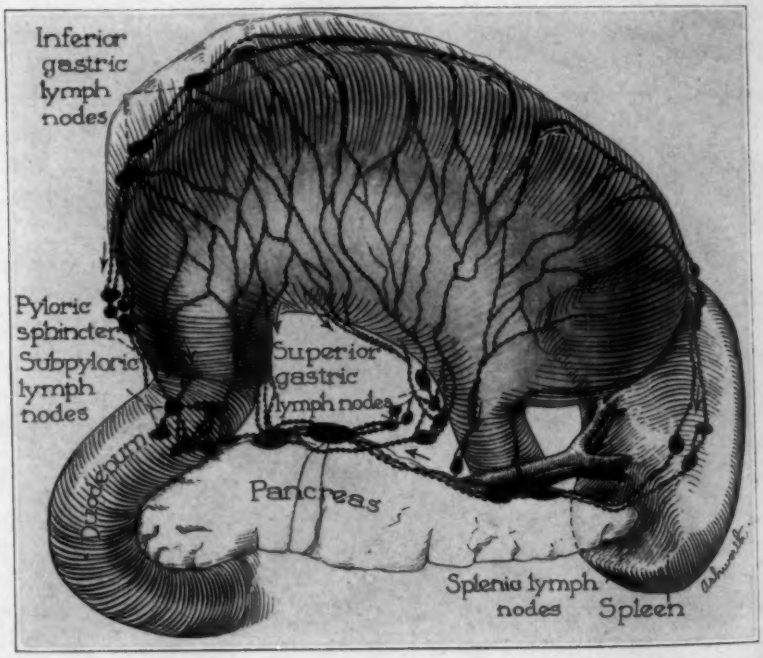


Fig. 14.—Lymphatic drainage of the stomach (posterior surface), as determined by injections into thirty-five specimens. There are four distinct areas of drainage. The arrows indicate the lines of drainage.

injection needle just distal to the pyloric sphincter. Pressures used here were similar to those used in injections above the sphincter. In each case, the injection medium stopped abruptly at the pylorus.

The lymphatic drainage of the stomach, as determined from these injections, is represented in figures 13 and 14. In figure 13 the drainage is represented by four distinct areas. The largest of these represents the area drained by the lymph nodes along the lesser curvature, and the flow of lymph is toward the cardia. The second most important area is that on the greater curvature; drainage is into the inferior gastric and subpyloric groups of lymph nodes. The third drains toward the splenic group of lymph nodes, and the fourth, which is relatively small, drains the superior distal portion of the pars pylorica to the right supra-pancreatic lymph nodes above the upper border of the pancreas. The collecting vessels from the fourth group may also drain into the biliary lymph nodes. In two specimens a direct communication between the pylorus and the so-called sentinel node at the hilus of the liver was observed. On the anterior surface of the gastrohepatic omentum were two or three small lymph channels which extended from the pylorus to a lymph node at the hilus of the liver. The drainage of the posterior surface of the stomach, represented in figure 14, corresponds with the areas described for the anterior surface. However, the boundaries of these areas of drainage must not be defined too acurately, for, if the normal drainage in a given direction is blocked, the injection medium readily flows in the opposite direction.

It should be emphasized that lymph vessels that seem to enter the lymph nodes are frequently only in contact with them on their way to more distant lymph nodes. This was repeatedly observed while the injections were being made into the specimen. The lymph node nearest the site of the initial injection was not necessarily the first node to be filled with the injection mass; the more distal nodes were frequently filled first. This was observed repeatedly along the lesser curvature of the stomach, and in other areas. In figure 15, the variations in the submucous lymphatic drainage at the pylorus are represented. The injection medium passes through the muscular layers of the pars pylorica either just proximal to the sphincter or, in rare instances, just distal to it, and then continues on the peritoneal surface of the duodenum toward the subpyloric lymph nodes, to the nodes above the upper border of the pancreas or, in rare instances, to the biliary lymph nodes. In one specimen (fig. 15*b*) an indirect communication between the lymphatics of the submucosa of the stomach and those of the duodenum was demonstrated. This indirect communication undoubtedly accounts for the fact that in cases of carcinoma arising in the pyloric canal, near the sphincter, carcinomatous ulcers may be found both proximal and distal

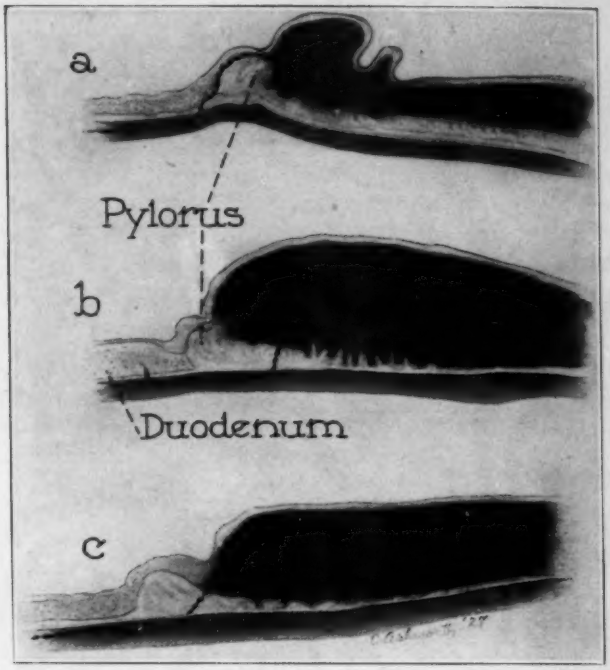


Fig. 15.—Lymphatic drainage at the pylorus, showing variations in the submucous drainage in this area.

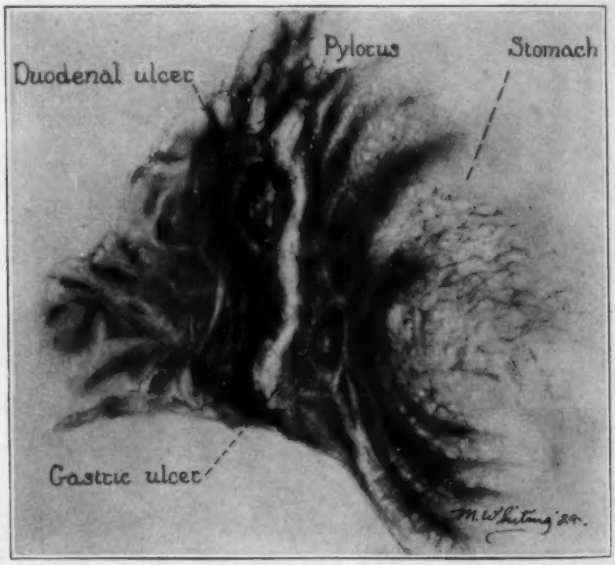


Fig. 16.—Carcinoma of the stomach. There are carcinomatous ulcers both proximal and distal to the pylorus, but the pyloric mucosa is still intact. (After Nagel.)

to the pyloric sphincter (fig. 16) with normal intact mucosa between the two ulcers. Nagel [37] reported a case in 1925. I made serial sections through the specimen and demonstrated that the two carcinomatous ulcers were connected by a relatively broad chain of carcinoma cells, along the lymphatic channel, as indicated in the indirect communication between the submucosa of the stomach and that of the duodenum.

Comment.—There can be no question but that there is a discontinuity between the submucous lymphatics of the stomach and those of the duodenum. This is explained by the presence of a connective tissue septum at the pylorus (fig. 17), which not only separates the submucosa

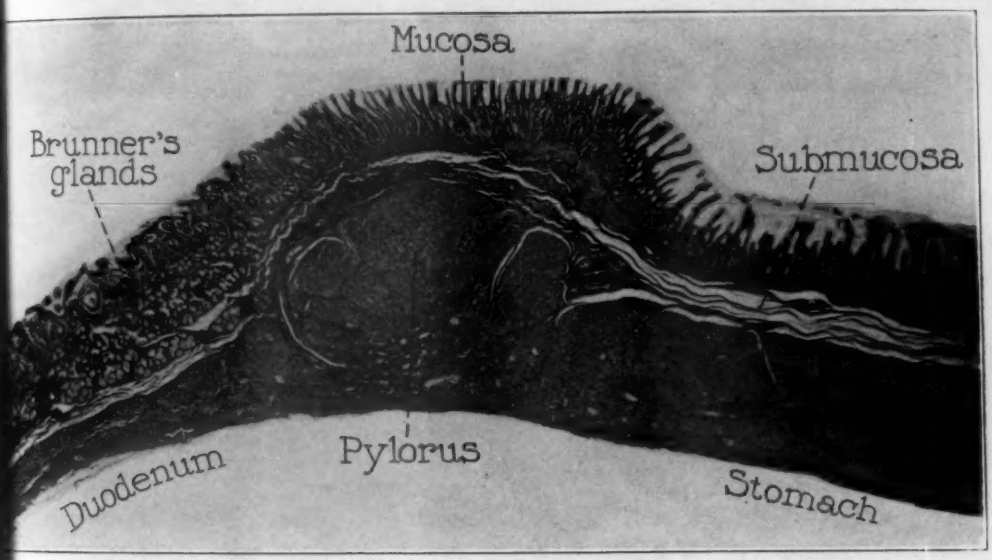


Fig. 17.—Longitudinal section through the posterior surface of the pylorus. The pyloric sphincter is well outlined, and a break in the circular musculature is seen distal to the pylorus. The subject was a boy, aged 6 months. (Reduced from × 18.)

of the stomach and duodenum, but also separates the circular musculature of the stomach from the corresponding circular coat in the duodenum. Thus at the pylorus there is a double barrier to the spread of carcinoma which is represented by the connective tissue septums and the discontinuity of the submucous lymphatics. This undoubtedly explains why carcinoma of the stomach, regardless of how extensive it may be, practically always stops at the pylorus and rarely, if ever, invades the duodenum (figs. 18 to 21). When extension in that direc-

37. Nagel, G. W.: Unusual Conditions in the Duodenum and Their Significance, Arch. Surg. **11**:529 (Oct.) 1925.

Fig. 18.—Annular carcinoma of the pyloric portion of the stomach. The growth extends up to the pylorus, where it stops abruptly. The duodenum was not involved. The specimen is from a male subject, aged 44 years.

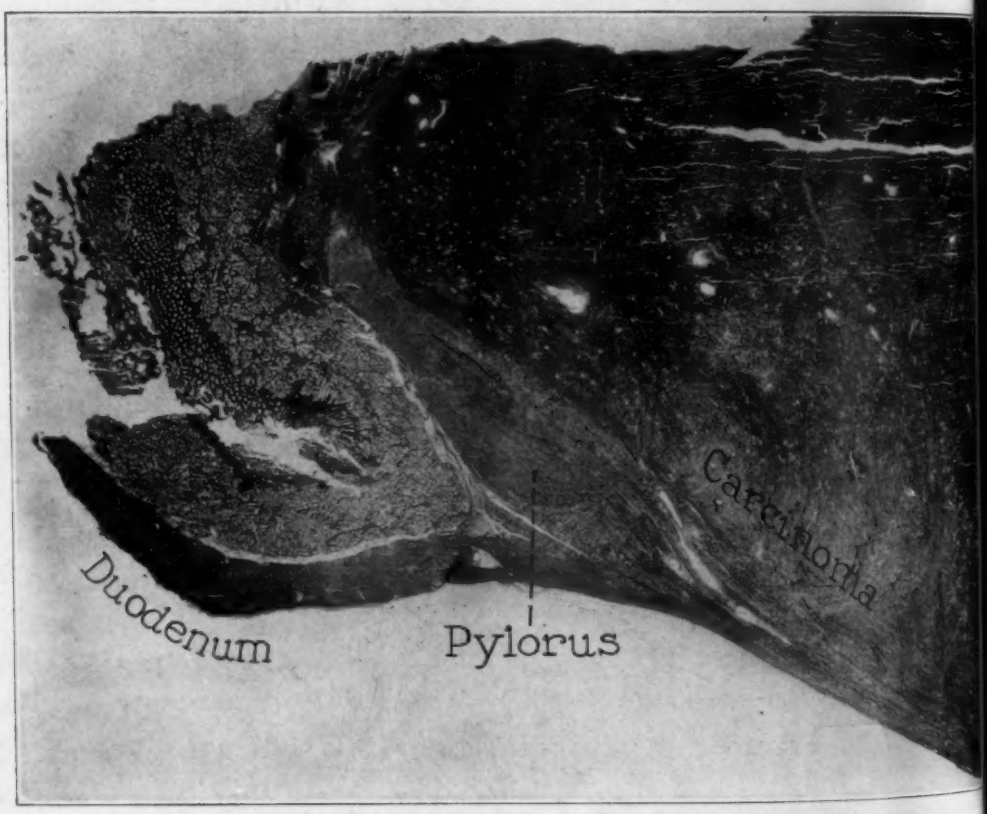


Fig. 19.—Longitudinal section through the pylorus of the specimen represented in figure 18. The pyloric sphincter is still intact, and the carcinoma stops abruptly at the sphincter.

tion does occur, it is usually along the peritoneal aspect of the duodenum, as indicated in figures 20 and 21. In figure 21, the carcinoma has extended along the submucosa of the stomach, up to the pylorus, and then through the muscle wall, and along the outside of the duodenum, thus following the lymphatic drainage as indicated in figure 15*c*. This line of drainage has been the usual one observed in all of the carcinomas studied, which includes a series of more than 200 cases. It should be remembered, however, that no barrier in the human body can hold out indefinitely against the invasion of carcinoma; and if the patient with an extensive carcinoma of the pars pylorica should live long enough, I feel sure that the duodenum eventually would be freely invaded. Of all the tissues in the body, connective tissue apparently offers the best resistance to the spread of carcinoma.

The ease with which the gelatin mass could be injected into the submucosa, in certain specimens, and the difficulties encountered in others are of marked interest, in view of the spread of carcinoma along this route. The variations in the density of the normal connective tissue in the region probably account for the fact that in some small carcinomas of the stomach there is extensive involvement of the adjacent lymph nodes, while in other cases in which relatively large carcinomas are present, there is little, if any, spread to the regional lymph nodes, even when the grade of malignancy, as determined by Broders' classification, is the same. Bothe [38] showed from a study of 100 cases that the size of the carcinoma bears no definite relation to the involvement of the regional lymph nodes. The largest growth he studied measured 14 by 11 cm., and the smallest, 2 by 1 cm. In spite of the difference in the size of these specimens, the smaller one showed involvement of all of the lymph nodes that were found with the specimen, whereas with the larger specimen only five of the fifteen nodes found were affected. These were resected specimens. This is in accord with the study of 200 cases previously made by MacCarty and Blackford.[39]

It should be remembered that nearly a third of all carcinomas occur in the stomach, and of these, 80 per cent are found in the pars pylorica (W. J. Mayo [40]). For this reason, exact knowledge of the lymphatic drainage of the stomach is of great practical importance. The curability of carcinoma depends largely on whether or not the lymph nodes are involved. Balfour and Hargis [41] recently showed that when the lymph

38. Bothe, F. A.: Lymphatic Involvement in Cases of Carcinoma of the Pyloric End of the Stomach, Surg. Gynec. Obst. **44**:761 (June) 1927.

39. MacCarty, W. C., and Blackford, J. M.: Involvement of Regional Lymphatic Glands in Carcinoma of the Stomach, Ann. Surg. **55**:811 (June) 1912.

40. Mayo, W. J.: Cancer of the Stomach: Its Surgical Treatment, Surg. Gynec. Obst. **14**:115 (Feb.) 1912.

41. Balfour, D. C., and Hargis, E. H.: Cancer of the Stomach, Am. J. M. Sc. **173**:773 (June) 1927.

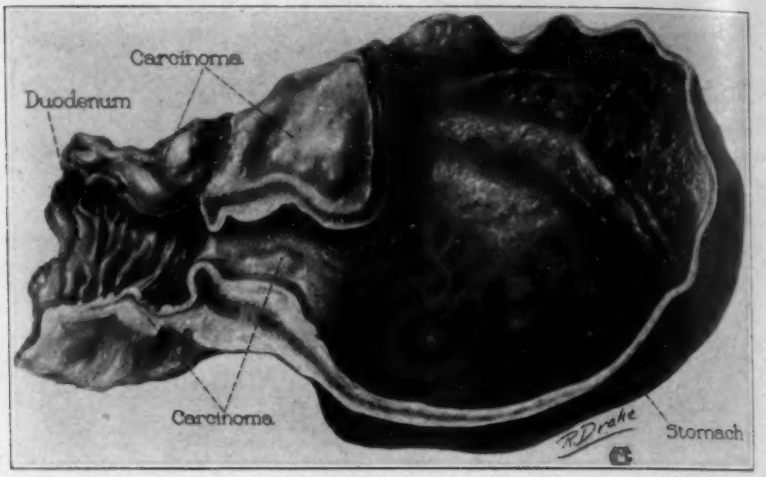


Fig. 20.—Carcinoma of the stomach. The growth extends to the peritoneal surface of the pars pylorica and duodenum. The duodenal mucosa is not involved. The specimen is from a male subject, aged 37 years.

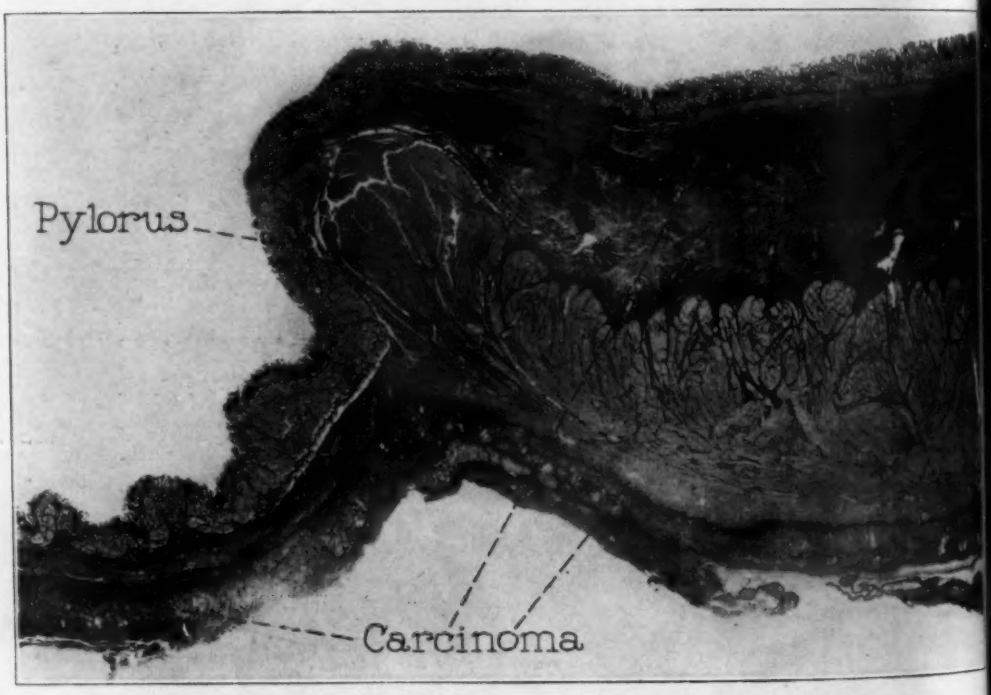


Fig. 21.—Longitudinal section through the pylorus of the specimen represented in figure 20. The submucosa of the stomach is distended with the infiltrating carcinoma which extends to the outside of the pars pylorica and duodenum. The duodenal mucosa is not involved.

nodes were not involved, 52 per cent of the patients were alive and well at the end of three years, whereas, when the lymph nodes were involved, only 19 per cent were alive and well at the end of three years. Another point worthy of emphasis is that in ordinary injections of the lymphatics of the stomach, it was observed that lymph vessels that seemed to enter lymph nodes were frequently only in contact with them on their way to more distant lymph nodes. This fact may explain why, in cases of carcinoma of the stomach, the surgeon often finds that the disease has missed the adjacent lymph nodes and has involved distant nodes. Resection for carcinoma should never be undertaken without careful exploration of the distant lymph nodes.

The possibility of the spread of carcinoma along the lymphatic channels which run with the pyloric artery should be emphasized. Studies at the Mayo Clinic (MacCarty and Blackford and Bothe) did not include this group, and Jamieson and Dobson were unable to find any reference in the literature to such a study. These lymphatic vessels drain a well marked region of the pylorus and are usually four or five in number. I have recently demonstrated this region of drainage in anesthetized dogs, by injection of india ink into the stomach, and it seems to be relatively larger in dogs than in man. The channels drain directly into the lymph nodes lying along the upper border of the pancreas. Frequently, one of these lymphatic vessels runs down the posterior surface of the duodenum to join the biliary lymphatic system. These vessels are not easy to remove in ordinary resections of the stomach. The possibility of a direct communication between the distal portion of the pylorus and the nodes at the hilus of the liver should be remembered, even though it was observed in only two of thirty-five specimens. There were two or three small lymph channels on the anterior surface of the gastrohepatic omentum, extending from the pylorus to the lymph node at the hilus of the liver. The usual procedure, therefore, in radical operations for carcinoma of the pyloric portion of the stomach can never give the surgeon absolute assurance that he has removed all of the first lymphatic relays.

SUMMARY

The continuity of the myenteric plexus from the stomach to the duodenum has been demonstrated by reconstruction models, and the possible significance of these data has been considered.

An investigation was undertaken to determine the lymphatic drainage of the stomach and the relationship between the lymphatics of the stomach and those of the duodenum. India ink and india ink and gelatin mixtures were injected into thirty-five specimens. In none of the specimens was there any demonstrable continuity between the submucous

lymphatics of the stomach and those of the duodenum. An indirect communication between the submucous lymphatics of the stomach and those of the duodenum has been demonstrated. In two specimens there was a direct communication between the pylorus and a lymph node at the hilus of the liver. The drainage of the stomach is represented by four distinct areas, the largest of which represents the area drained by lymph nodes along the lesser curvature; the second most important is that on the greater curvature which drains into the inferior gastric and subpyloric groups of lymph nodes. The third drains toward the splenic group of nodes, and the fourth drains the distal portion of the pars pylorica to the nodes above the pancreas.

ATTITUDES ASSOCIATED WITH LESIONS ABOUT THE HIP JOINT *

VERNON L. HART, M.D.
ANN ARBOR, MICH.

One may frequently gain considerable information from a careful study of the position of deformity or attitude of the lower extremities associated with lesions involving the hip joint. A characteristic gait not infrequently enables one to suspect a certain lesion, and it is not uncommon for one to suspect a definite lesion of the hip joint from careful inspection alone without resorting to further examination by palpation, manipulation, measurements, muscle tests, roentgen and laboratory tests, since certain lesions about the hip joint are manifested by more or less characteristic attitudes. The purpose of this paper is not to point out that the observation of the position of deformity or attitude of the lower extremities will make possible a "snap" diagnosis, but to emphasize the fact that such an observation may aid in the differential diagnosis and in determining further examination necessary to arrive at a correct opinion. The internist may be encouraged to resort to special tests after the observation of a characteristic blood picture, or the ophthalmologist may be directed along a definite course of investigation after noting certain alterations in the fundus. Although a gait, a blood picture, a change in the fundus or an attitude may be a fairly constant manifestation of a certain lesion, it does not justify disregard of the fundamental teaching that before instituting treatment a positive diagnosis should be established when possible by a complete examination exhausting all necessary clinical and laboratory tests.

The particular attitude or position of deformity of the lower extremities should be recognized during the first part of the examination, the period of inspection. It is important to understand certain fundamental principles involved in the examination of the lower extremities. Before one can state definitely the position of the extremities, it is essential to determine the position of the pelvis and the lumbar spine. For instance, a patient may appear to lie in bed with an extremity held in abduction, but careful examination will demonstrate that the hip is actually in a position of adduction (figs. 1 *A* and *B*). The apparent abduction is the result of a tilting or rotation of the pelvis on its anteroposterior axis. In the same way, rotation of the pelvis on its vertical axis may

* Submitted for publication, May 2, 1930.

* From the Department of Surgery, Division of Orthopedics, University of Michigan Hospital.

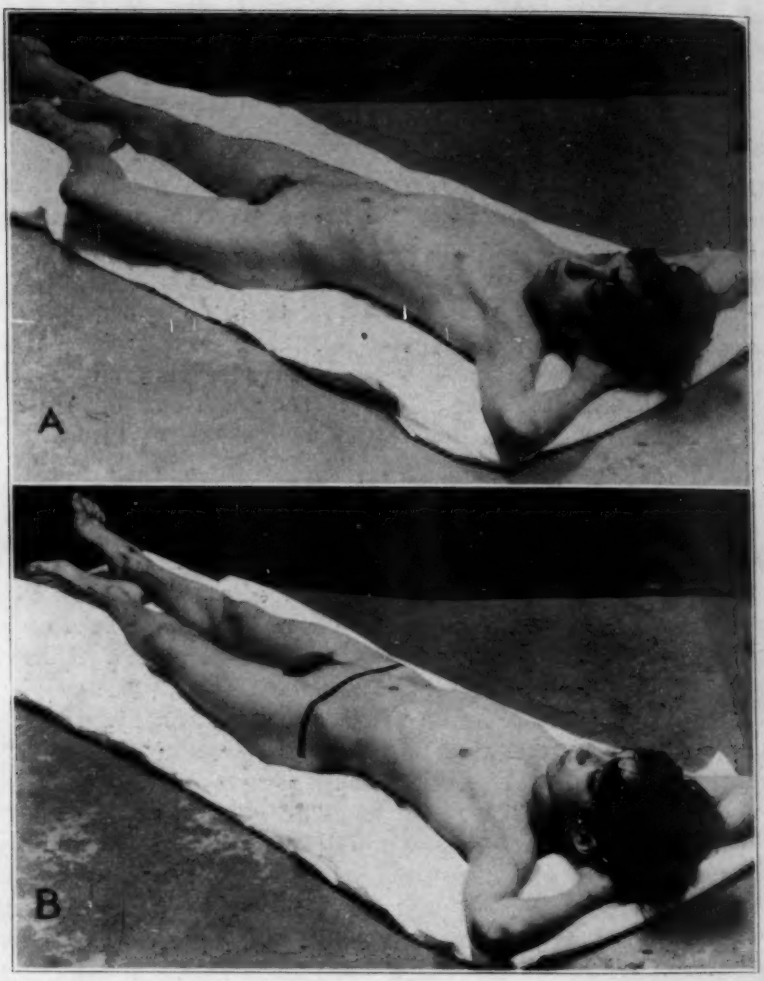


Fig. 1.—In *A*, the attitude of the left lower extremity appears to be abduction and external rotation. Actually, the extremity is in a position of adduction and external rotation which is determined only when the pelvis is placed on a transverse and horizontal plane (see fig. 1 *B*). In *B*, the same patient is seen as in figure 1 *A*, with the pelvis on a transverse and horizontal plane revealing the correct attitude of adduction and external rotation.

result in a faulty interpretation of the degree of internal or external rotation of an extremity. A correct interpretation of the position of deformity of an extremity can be made only when the pelvis is placed on a transverse and horizontal plane without rotation on either its vertical or horizontal axis. The presence of a flexion deformity of the hip joint cannot be determined by inspection of the involved extremity alone, since it may be masked by the development of a compensatory lumbar lordosis (figs. 2 *A* and *B*). It is best to examine a patient on a

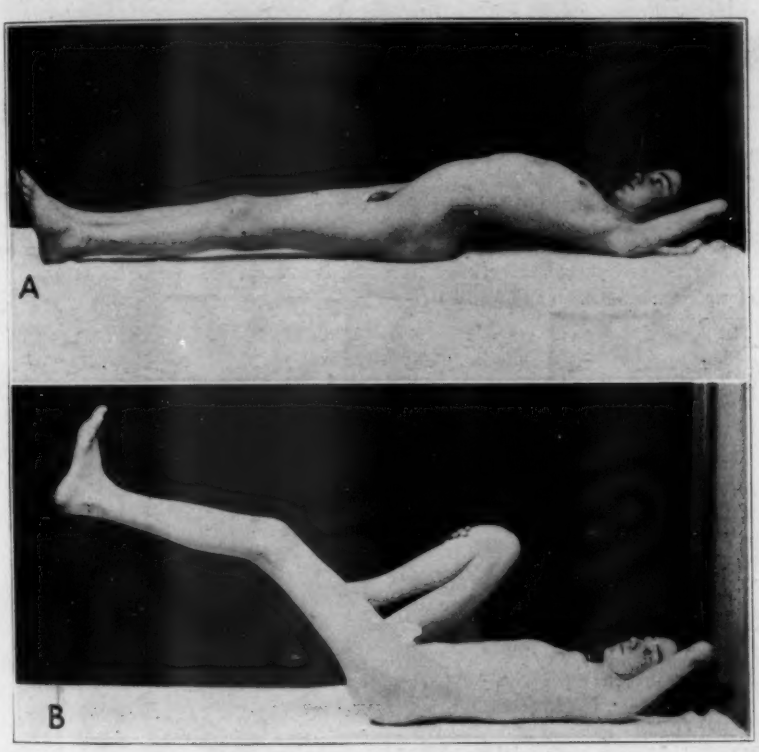


Fig. 2.—In *A*, the 45 degree flexion deformity of the hip is not apparent because of the presence of a compensatory lumbar lordosis. In *B*, obliteration of the lumbar lordosis by approximating the right knee to the chest makes the flexion deformity of the left hip apparent.

firm mattress or examining table in order to have the pelvis and lumbar spine under control.

The position of deformity assumed by the involved extremity depends upon many factors, namely: muscle spasm, muscle paralyses, muscular incoordination, disturbed muscle balance and mechanical alterations following trauma, joint distention, simple joint irritation, joint destruction, gravity, pain and instinctive efforts of the patient to gain comfort.

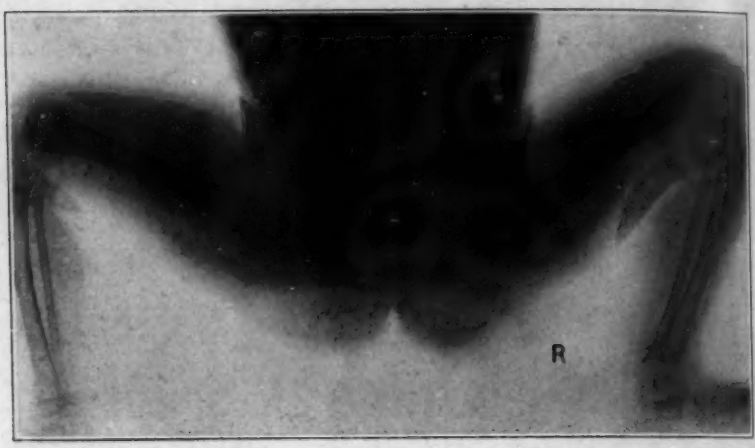


Fig. 3.—"Frog attitude" assumed during the acute stage of infantile scurvy. Note the subperiosteal hemorrhage over the lower portion of the right tibia and the epiphyseal halos. (See fig. 4.)

Fig. 4.—Functional position of the lower extremities following correction of the frog attitude. Note calcification of the massive subperiosteal hemorrhage encircling the shaft of the right femur.

The attitude may be the result of one or of a combination of several of the foregoing factors, and it may change during the course of a disease if one factor gradually assumes a more important rôle, replacing the effect of another. For instance, a position of comfort in abduction may be replaced by the position of adduction following the development of muscle spasm.

A classification of lesions about the hip joint that present fairly constant atitudes may be outlined according to age periods, since certain diseases affecting the hip joint manifest their clinical onset during definite age periods (see table). The pseudoparalyses of rickets, scurvy

Attitudes Associated with Hip Joint Lesions

Age Period of Infancy	Age Period of Childhood	Age Period of Adolescence
Pseudoparalyses of Rickets Scurvy Syphilitic epiphysitis	(a) Tuberculosis of hip joint Flexion { Adduction, internal rotation / Abduction, external rotation }	Separation of upper femoral epiphysis Adduction and external rotation
Frog attitude	(b) Spontaneous dislocation of hip joint Flexion, adduction, internal rotation	
	(c) Acute septic arthritis of hip joint Flexion { Adduction, internal rotation / Abduction, external rotation }	
	(d) Chronic deforming arthritis (Still's disease) Flexion (adduction, internal rotation)	

Age Period of Early Adult Life	Age Period of Late Adult Life
(a) Spondylitis deformans (Rhizomelic) (Bent ankylosed position) Flexion, adduction of hips Flexion or extension of spine	(a) Malum coxae senilis Flexion, adduction, external rotation
(b) Traumatic dislocation of hip joint Anterior dislocation— Flexion, abduction, external rotation Posterior dislocation— Flexion, adduction, internal rotation	(b) Fracture of neck of femur Adduction, external rotation

and syphilitic epiphysitis are observed during the period of infancy. Septic arthritis of the hip, primary or secondary to a remote infection, may appear at any age, but is most common during the periods of childhood and adolescence. The chronic deforming arthritides that present quite constant attitudes of the lower extremities are Still's disease and spondylitis rhizomelica, which have their onset of symptoms during the periods of childhood and early adult life, respectively. The greater number of cases of tuberculosis of the hip begin during the period of childhood, although they may appear at any age. Spontaneous dislocation of the hip joint may occur during any age period, but the majority of cases develop during the period of childhood. Epiphyseal

coxa vara, or separation of the upper femoral epiphysis, invariably begins during the period of adolescence. The onset of symptoms in most cases is at about the age of 14 years. Traumatic dislocation of the hip joint is most frequently seen during early adult life, when exposure to severe trauma is more common. "Malum coxae senilis," or chronic hypertrophic arthritis localized to the hip joint, is, as the name implies, a disease of late adult life. Fracture of the femoral neck is usually an injury of old age, though it may occur at any time.

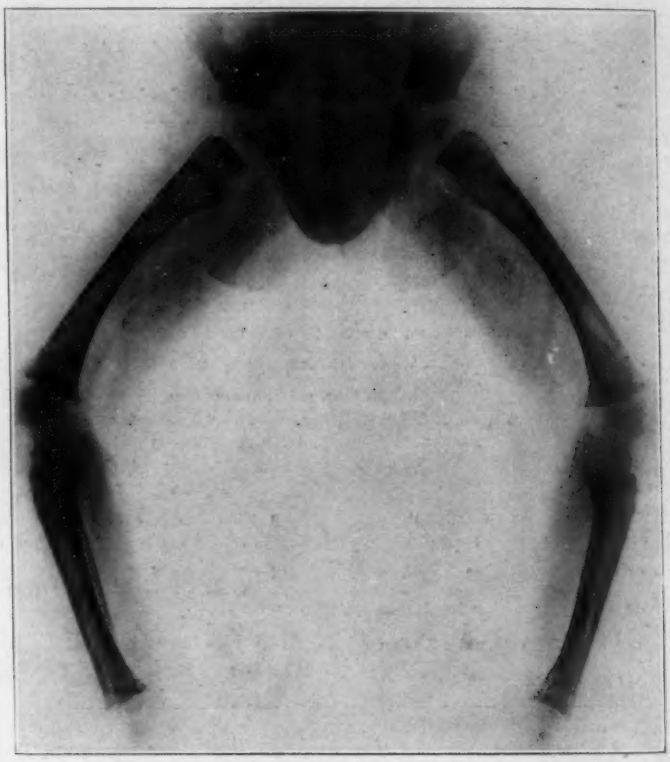


Fig. 5.—This attitude resulted from the development of contractures about either hip as the patient lay in the frog attitude during the acute stage of rickets. Functional position of the hips was readily obtained by skin traction. Note the flaring of the femoral shafts at the epiphyseal disk regions and the increased density of the femoral shafts on the concave sides.

I have observed four children who were admitted to the clinic with the lower extremities in the typical "frog" position (flexion 90 degrees, abduction 90 degrees and external rotation 90 degrees). Clinical and roentgen examination demonstrated evidence of active rickets in two cases and early infantile scurvy with subperiosteal hemorrhages in one

case (figs. 3 and 4). The lower extremities of three of these children were tender on palpation and painful on manipulation, clinically manifested by pseudoparalyses. The fourth child was admitted to the clinic with the lower extremities fixed in the "frog" attitude as a result of contractures about the hips (fig. 5). Examination showed evidence of healed rickets, and it was assumed that the child lay in the "frog" position during the active tender stage of rickets with subsequent development of contractures resulting in a fixed deformity. Adhesive traction was applied to the lower extremities over a period of several

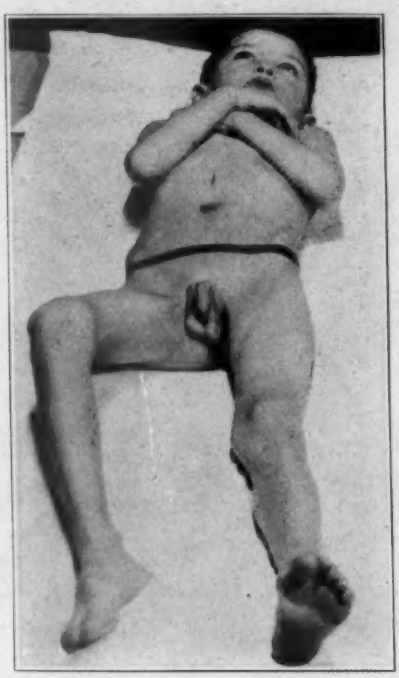


Fig. 6.—Flexion, abduction and external rotation attitude assumed during the early stage of tuberculosis of the right hip joint with an insidious onset.

weeks, and complete correction was gradually obtained. This case clearly demonstrated the importance of early correction of the "frog" attitude during the stage associated with pseudoparalyses to prevent the development of a fixed deformity. This is easily accomplished by proper adjustment of pillows or sand bags or adhesive skin traction maintaining the lower extremities in the optimum position for return of function.

Congenital syphilis may be manifested as an acute syphilitic epiphysitis of the hips associated with pseudoparalyses—the pseudoparalyses of Parrot. The lesion occurs along the line of ossification in long bones

and resembles the epiphyseal disturbance of rickets. Undoubtedly the "frog" attitude may be assumed during the acute and tender stage of this disease when associated with pseudoparalyses. I have never observed this lesion. In general, the observation of the "frog" attitude during the age period of infancy should suggest rickets, scurvy or acute syphilitic epiphysitis with pseudoparalyses.

Malposition is one of the most common evidences of tuberculosis of the hip joint. The attitude of the involved extremity varies according to the stage of the disease and whether the onset is insidious or acute. When the onset is insidious, the malposition usually observed during the early stage when there are symptoms of simple irritation of the

Fig. 7.—This photograph may illustrate either instinctive traction applied to the left lower extremity or a method used by the patient to immobilize the right lower extremity. (Patient with tuberculosis of the right hip joint.)

joint with effusion is flexion, abduction and external rotation (figs. 6 and 7). Late in the disease when there is definite involvement of the cartilage and destruction of the joint the malposition, as a rule, is flexion, adduction and internal rotation (figs. 8, 9 and 10). The acute tuberculous hip is held in flexion, associated with either abduction and external rotation or adduction and internal rotation. The flexion deformity is a constant malposition; abduction is always associated with external rotation and adduction with internal rotation. The factors that determine the malposition in an individual case cannot be satisfactorily determined.

Spontaneous or pathologic dislocation of the hip joint more commonly observed during early life, presents a fairly constant malposition of the involved extremity in flexion, adduction and internal rotation. The position is one of instability and is productive of dislocation (figs. 11 and 12). The mechanism of production of spontaneous dislocation is a derangement of the normal action of the muscles surrounding the hip joint and is not dependent on destruction of bone or ligament. The normal muscular arrangement about the hip joint may be altered by muscle spasm, which is always present during the acute stage of infection of the hip joint, flaccid paralyses of anterior poliomyelitis and

Fig. 8.—Flexion, adduction and internal rotation attitude associated with late tuberculosis of the left hip joint with complete destruction of the femoral head and the formation of a wandering acetabulum.

muscle incoordination in spastic paralysis. This attitude is a dangerous one and should be recognized early and corrected before the occurrence of the dislocation. The attitude is easily overlooked early in the disease unless the position of the pelvis and lumbar spine are carefully studied. The patient may lie in bed with the legs parallel; however, one extremity may be in marked adduction with the pelvis rotated on its anteroposterior axis, and if unrecognized a faulty interpretation of the attitude is made. Also the flexion deformity may not be apparent because of the development of a compensatory lumbar lordosis. Early recognition of

"the position of instability" should be emphasized because of the frequent resulting spontaneous dislocation of the hip which is preventable but when once established is corrected with much difficulty. It is a fundamental principle that a patient with an acute infection of the hip

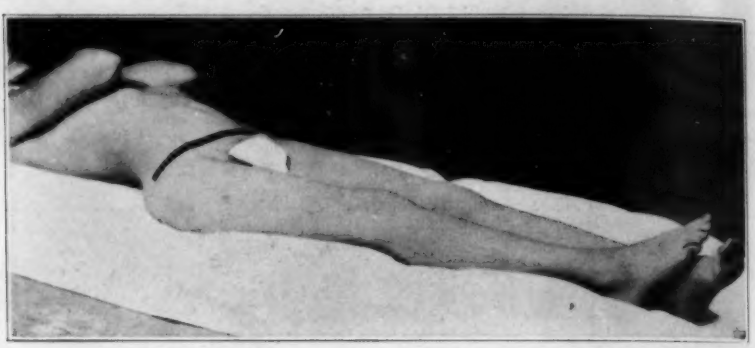


Fig. 9.—Late tuberculosis of the hip. The flexion deformity is masked by a compensatory lumbar lordosis.

Fig. 10.—Same as figure 9.

joint should be properly arranged in bed either on a firm mattress or on a Bradford frame so as to have the pelvis and lumbar spine under control. The pelvis should be on a transverse and horizontal plane and the lumbar spine flat. It is often useful to mark the skin with an ink line or to place a colored adhesive tape between the two anterior superior

Fig. 11.—Purulent hip joint in position of stability flexion and abduction. Note the pathologic, epiphyseal separation with slight displacement.

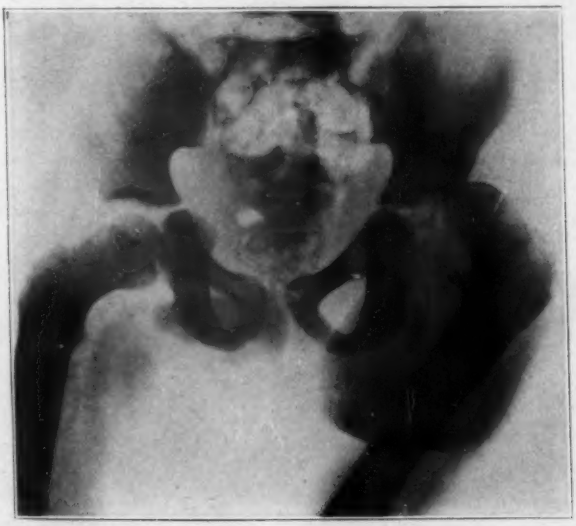


Fig. 12.—Same case as in figure 11, one day later, with hip joint in "position of instability," flexion and adduction, resulting in spontaneous dislocation.

Fig. 13.—Attitude of flexion, abduction and external rotation associated with septic arthritis of the right hip joint.

Fig. 14.—Roentgenogram of patient in figure 13, demonstrating the attitude of flexion, abduction and external rotation associated with septic arthritis of the right hip joint.

Fig. 15.—Chronic deforming arthritis or Still's disease with flexion deformities of the hip joints. Note the flexion, adduction and internal rotation attitude or "position of instability" of the left lower extremity with resulting spontaneous dislocation of the left hip.

Fig. 16.—Same as figure 15.

Fig. 17

Fig. 18

Fig. 17.—Bent ankylosed attitude in spondylitis rhizomelica or ankylosing arthritis of the spine and hip joints.

Fig. 18.—Same as figure 17.

Fig. 19.—Same as figure 17.

Fig. 20.—Epiphyseal coxa vara or separation of the upper femoral epiphysis which is invariably associated with adduction and external rotation deformity of the involved extremity. (See figure 21.)

Fig. 21.—Separation of the upper femoral epiphysis with adduction and external rotation attitude of the involved extremity.

spines while the patient is under treatment so that the position of the pelvis may be readily recognized. It is also a fundamental principle that during the acute stage of any infection of the hip joint "the position of

Fig. 22.—Adduction and external rotation attitude associated with fracture of the femoral neck. (See figure 23.)

Fig. 23.—Nonunion fracture of the left femoral neck with adduction, external rotation attitude of the involved extremity.

instability" (flexion, adduction, internal rotation) should be prevented, and if present should be corrected to the position of stability by means of skin traction. The knee should always be supported in a position of slight flexion, since continued traction on an extremity with the knee in

complete extension is productive of hyperextension deformity of the knee or genu recurvatum.

Septic arthritis of the hip joint, either primary or secondary to some remote source of infection, is in most instances associated with the position of flexion, abduction and external rotation (figs. 13 and 14), although the flexion deformity may be combined with adduction and internal rotation. An attempt at traction on the involved extremity by the foot of the opposite normal extremity is frequently observed, an instinctive, unconscious effort at traction for the purpose of relieving

Fig. 24.—Flexion, abduction and external rotation attitude associated with traumatic anterior dislocation of the hip.

muscle spasm and pain. Subsequent involvement of the normal hip joint in this group of cases is common, and late in the disease a bilateral infection of the hip joint is observed with the primarily involved hip in the position of stability and the hip joint of the opposite extremity, which was utilized for instinctive traction, in the position of instability. In this group with bilateral involvement of the hip joint the primarily affected hip never goes out of place, since the position is one of stability, but the hip joint of the opposite side which was placed in "the position of instability" during an effort at instinctive traction is frequently dislocated. The instinctive effort at traction by the normal extremity may also be observed during the acute stage of tuberculosis of the hip joint,

when the involved extremity is held in flexion, abduction and external rotation.

Still's disease or chronic deforming polyarticular arthritis of childhood presents a constant malposition of the lower extremities. The

Fig. 25.—Traumatic anterior dislocation of the hip with flexion, abduction and external rotation attitude of the involved extremity.

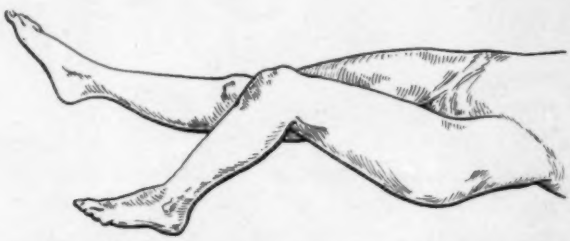


Fig. 26.—Flexion, adduction and internal rotation attitude associated with traumatic posterior dislocation of the hip.

hips are flexed, adducted and internally rotated. Flexion is the most prominent deformity, but adduction and internal rotation are often combined and frequently more marked in one extremity, placing it in "the position of instability" which may result in spontaneous dislocation

(figs. 15 and 16). Flexion and subluxation deformities of the knees and equinus deformities of the feet are also commonly associated.

The attitude of an advanced case of spondylitis deformans of the rhizomelic type is also typical. The dorsal and lumbar spine may be ankylosed in complete extension or greatly curved in the form of an arc. When the cervical spine is ankylosed, the head may be either flexed on the trunk or in complete extension. The hip joints ankylose in flexion, often associated with varying degrees of adduction. The bent ankylosed position in rhizomelic spondylitis is characteristic (figs. 17, 18 and 19).

Fig. 27.—Traumatic posterior dislocation of the hip with flexion adduction and internal rotation attitude of the involved extremity.

Epiphyseal coxa vara, or separation of the upper femoral epiphysis, which invariably has its onset of symptoms during the age period of adolescence, presents a typical attitude (figs. 20 and 21). The involved extremity is adducted and externally rotated. Flexion deformity of the involved hip is not constant, which is in contrast to the condition found in infections of the hip joint in which varying degrees of flexion are practically always found. Separation of the upper femoral epiphysis is a hazard of adolescent life while fracture of the neck of the femur is a hazard of late adult life, and the attitude of the involved extremity in each condition is very similar. In old persons with fracture of the

femoral neck, the attitude is typical (figs. 22 and 23). The extremity is adducted and externally rotated. The external rotation is often marked, and when the extremity is passively rotated inward and then released it immediately returns to the former position.

Traumatic dislocation of the hip joint is either anterior or posterior and each type is associated with a typical attitude. Anterior dislocation is characterized by the position of abduction and external rotation with the knee flexed (figs. 24 and 25). When the femoral head lies in the

Fig. 28.—Flexion, adduction and external rotation associated with malum coxae senilis of the left hip.

obturator foramen, the external rotation is less marked while abduction is increased. If the femoral head occupies the pubic position, the external rotation is more marked and abduction is decreased. There is also associated with it a mild flexion deformity. Posterior dislocation presents an attitude of flexion, adduction and internal rotation (figs. 26 and 27). The heel of the dislocated extremity often rests on the dorsum of the opposite foot. The attitude is less pronounced when the dislocation is

of the low type with the femoral head in the region of the greater sciatic notch.

Malum coxae senilis or hypertrophic arthritis of the hip joint, which appears at or after middle adult life, is characterized by the attitude of flexion, adduction and external rotation (figs. 28 and 29). Flexion and adduction are the most marked features of the attitude. There is occasionally a definite history of injury preceding the onset. The history of injury during old age and the foregoing attitude may suggest fracture of the neck of the femur, but complete examination will establish the diagnosis of osteo-arthritis of the hip joint.

Fig. 29.—Malum coxae senilis of the left hip with flexion, adduction and external rotation attitude of the involved extremity. Note the loss of joint space, sclerosis and areas of cystic degeneration of the femoral head and acetabulum.

SUMMARY

1. The attitudes of the following lesions about the hip are discussed, namely: infantile scurvy, rickets and syphilitic epiphysitis associated with pseudoparalyses; tuberculosis of the hip; spontaneous or pathologic dislocation of the hip; septic arthritis of the hip; chronic deforming arthritides—Still's disease and spondylitis rhizomelica; epiphyseal coxa vara or separation of the upper femoral epiphysis; traumatic dislocations of the hip; malum coxae senilis or hypertrophic arthritis of the hip, and fracture of the neck of the femur.

2. Certain lesions about the hip joint present fairly constant attitudes of the lower extremities and have definite relations to age periods.

3. There are a number of factors that determine the attitude of the lower extremities; the factors that determine the malposition in an individual case cannot always be satisfactorily explained.

4. A correct interpretation of the attitude of the lower extremities cannot be made unless the pelvis is placed in the normal anatomic position with reference to the transverse and horizontal planes, and the lumbar spine is flat.

5. The "frog" attitude in a child should lead the physician to suspect one of the pseudoparalyses associated with rickets, scurvy or syphilitic epiphysitis.

6. "The position of instability" of the hip joint (flexion, adduction, internal rotation) is productive of spontaneous dislocation and should be considered a dangerous attitude.

7. Epiphyseal coxa vara is a hazard of adolescent life, and fracture of the neck of the femur is a hazard of old age. The attitude of the involved extremity in each condition is similar, i. e., adduction and external rotation.

8. Infection of the hip joint presents a constant malposition of flexion combined with either abduction and external rotation or adduction and internal rotation.

SPONDYLITIS DEFORMANS*

SAMUEL KLEINBERG, M.D.
NEW YORK

One of the greatest advances in orthopedic surgery is the development and application of preventive measures in the control of deformities, particularly those of the spine. Because of familiarity with the progress and end-results of certain diseases, it is possible to institute treatment to forestall severe deformities and their inevitable accompanying functional derangement. One is no longer content to watch a case of structural scoliosis, for instance, treated by antiquated therapy, progress to a degree of deformity which is both grotesque and disabling. By a well planned spinal fusion, the mild and moderate grades of scolioses may be prevented from becoming worse, thus assuring the patient an acceptable appearance and physical fitness. Similarly, the progressive deformity of spondylitis deformans may be checked if the disease is recognized in its incipiency and the proper course of treatment immediately instituted. The purpose of this communication is to call attention to the clinical aspects and to the most effective form of treatment in cases with increasing deformity.

Spondylitis deformans is a progressive disease of the spine characterized by gradually increasing flexion of the trunk and ankylosis of the vertebrae. The disease may come on insidiously, but it usually begins suddenly with pain and stiffness of the back, resembling an attack of so-called lumbago. The pain may be limited to one part of the spine, or may be general throughout the back. It may radiate to the head, chest, abdomen or to the extremities. At first the symptoms appear at intervals of varying duration, with intermissions, during which the patient is free from discomfort and stands and walks erect. Injury or illness may aggravate the symptoms. If the patient is examined during the first year or two after the onset, it will be found that he stands and walks with his head bent forward. The back is symmetrical but flat. There is a loss of the normal lumbar hollow, and the spinal motions are moderately or markedly limited. If asked to straighten up, the patient sways his trunk backward until his eyes look forward. The surgeon can, however, readily detect that in this act there is only slight motion in the spine itself, the trunk being hyperextended on the hips. There is

* Submitted for publication, May 2, 1930.

* Read at a meeting of the Clinical Society of the Hospital for Joint Diseases, April 8, 1930.

moderate spasm of the trunk muscles, but no tenderness of the vertebrae. When the trunk is bent forcibly in any direction, there is considerable pain. This is, I believe, a significant observation, indicating inflammatory irritation of, or in the vicinity of, the vertebrae. An x-ray film of the spine may be entirely negative or may show marginal lipping or osteophytes. This may not excite special interest, unless one suspects the true nature of the lesion and anticipates that continued growth of the bony spurs will cause fusion of the vertebrae. Because of the slow progress of the disease and the frequent remissions and periods of well being, the attention of both the patient and his physician does not become focused on the spine until there is a definite resistant deformity. When the orthopedic surgeon is consulted, several years have usually elapsed since the onset of the symptoms; there are well marked clinical evidences

Fig. 1.—A patient with an advanced degree of spondylitis deformans. The trunk is fixed in flexion. The chest is flat and the abdomen prominent. There is marked increase in the dorsal backward curve. The head is held forward. The patient cannot look up except by bending the trunk backward on the hips. Note the crease across the abdomen indicating flexion of the trunk.

of grave disturbance of the function of the spine, and the x-ray films reveal the beginning of ankylosis of the vertebrae.

At a later stage there is increasing deformity with stiffness of the back and weakness of the back and legs. The trunk appears bent on itself (fig. 1). There is a forward thrust of the head, so that the eyes are continuously directed downward. There is a marked increase in the backward curve of the dorsal area and flattening of the lumbar spine. The lower part of the chest is depressed. The lower part of the abdomen bulges, and there is a deep crease across the upper part of the abdomen indicative of fixed flexion of the spine. The fixed flexion deformity becomes especially noticeable when the patient lies on his back. When the lumbar area is flat on the table, the head is from 4 to 8 inches (10.16 to 20.32 cm.) away from the table. The gait is

awkward because of the rigidity of the spine during every motion of the body. Ultimately the spine becomes completely ankylosed, so that the patient has what is called a "poker back." He is usually able to move his head backward and forward a little because the occipito-atloid

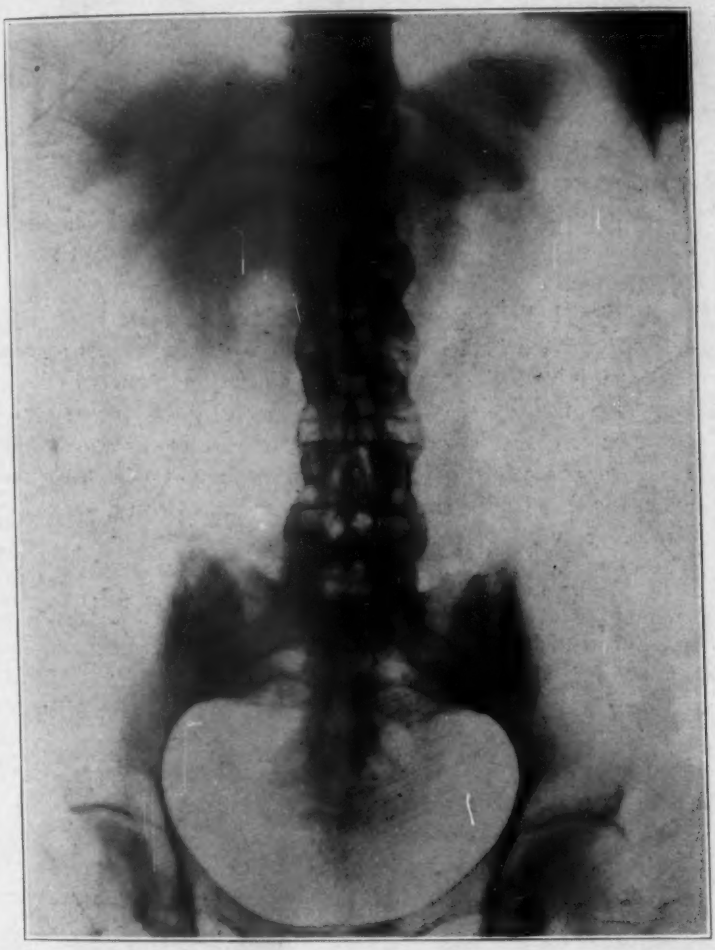


Fig. 2.—Anteroposterior view of the lumbar spine in a case of advanced spondylitis deformans showing complete bony ankylosis of the spine by bilateral intervertebral bridges of bone.

joints are rarely involved, but he cannot move his head sideways, nor bend his spine forward, laterally or in a rotary direction. The ribs may become fixed through ankylosis of the costovertebral joints, so that breathing is entirely abdominal. The general health of the patient is very poor, and he suffers much from headache and neurasthenia. The

backache disappears when the vertebral ankylosis is complete, but the pain in the limbs may continue indefinitely because of the pressure of the newly formed bone on the nerves at their exit from the intervertebral foramina.

Spondylitis deformans may occur in one of three forms: (1) as an independent disease (most frequent type), (2) as part of a general polyarthritis and (3) in association with involvement of the hips or shoulders. It occurs much more frequently in males than in females, and usually between the ages of 20 and 40. Its causes are numerous, and many of them are not thoroughly understood. In general, three etiologic types may be distinguished: (1) that which is part of a general metabolic disturbance, (2) the traumatic variety and (3) the infectious group. In the latter type are such well known causes as typhoid and gonorrhea.

The chief pathologic change is a chronic progressive ossifying periostitis of the spine which leads to ankylosis of the vertebrae and the costovertebral joints. This process may affect a limited area, but it usually involves the entire spine, and is apparently the same irrespective of the particular etiologic factor. The new bone in the advanced stage of this disease, according to Jones and Lovett, appears in the x-ray picture like callus that has been melted and allowed to run down the front and sides of the vertebral column (fig. 2).

TREATMENT

The treatment is general and local. The general treatment is directed toward removing or remedying whatever etiologic factor or focus of infection is discovered, toward improving the health of the patient and toward relieving him of pain. So far as focal infection is concerned, it has been my experience that one can rarely discover a source of infection that may with certainty be considered the real cause of the spinal disease. Furthermore, removal of infectious foci, such as diseased tonsils or teeth, does not usually have a beneficial effect on the vertebral lesion. This fact was emphasized in a recent article on spondylitis deformans by Dr. Nachlas [1] of Baltimore. In the foregoing thought, I do not mean to convey the impression that spondylitis deformans is not dependent on some infectious process. But, thus far, I have been unable, except in a few cases in which the disease was evidently of typhoid or gonorrheal origin, to identify definitely the causative factor.

The local treatment is directed to the back and has practically no relation to the cause of the disease. The local treatment of spondylitis

1. Nachlas, William: Focal Infection in Spondylitis Deformans, Arch. Surg. **20**:159 (Jan.) 1930.

deformans is concerned first, with the correction of the deformity, secondly, the mobilization of the spine whenever possible, and thirdly, the relief of backache. When the condition of the patient has progressed to the stage of complete bony ankylosis of the vertebrae, the deformity and disability are permanent and irremediable. However, during the earlier stages, and for a long time before the ankylosis is complete and absolute, there is ample opportunity to apply treatment effectively. Though the patient may present what appears to be clinically complete rigidity and fixation of the entire spine, if the x-ray picture shows no bony ankylosis or complete fusion of only some of the vertebrae or partial fusion of several small spinal segments, I am encouraged to apply treatment in the hope of arresting the process and, more particularly, of correcting the existing deformity. It is this phase of spondylitis

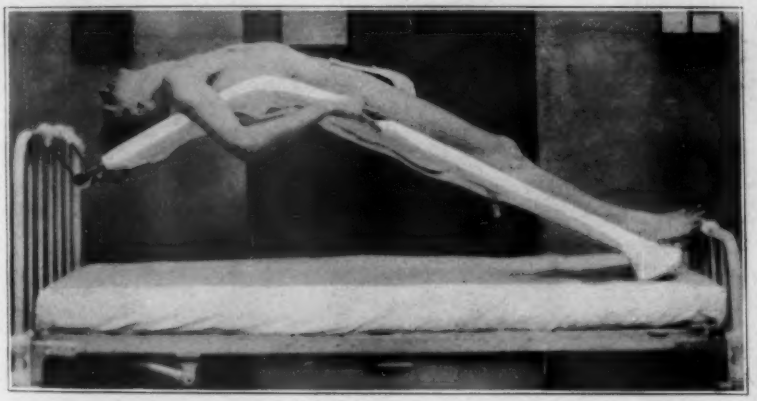


Fig. 3.—Patient with spondylitis deformans resting on a convex frame. This attitude of hyperextension is attained only after several weeks of treatment on a frame which at first is flat and later is gradually made convex.

deformans that has interested me especially, and I shall discuss at length the local treatment which has proved of great value.

The essential element in the treatment is continuous rest in the supine position, first on a straight frame and later on a convex frame (fig. 3). In this attitude the muscles relax, the discomfort disappears, and the spine gradually adapts itself to the curve of the frame. The treatment is slow and prolonged. Both patient and surgeon must be prepared to spend from two to six months in attaining their object. The treatment can best be carried out in a hospital equipped with a brace shop for the manufacture of the frame and for the frequent changes in its angulations. The treatment is most conveniently carried out in an orthopedic institution, where everybody concerned is accustomed to chronic cases and the care of this type of patient, who needs much patient nursing,

The frame is rectangular, made of gas pipe and covered with tightly stretched canvas. It is the ordinary convex frame used for scoliosis, round shoulders and Pott's disease, except that it is several inches wider than the distance between the patient's shoulders, so that his arms may rest comfortably on the canvas. Twenty inches (50.8 cm.) is an average width. The length of the frame is sufficient to allow it to extend about 4 inches (10 cm.) above the patient's head and at least as much below his feet. The frame may rest on the mattress or be suspended from the head and foot pieces of the bed.

Usually the patient cannot be placed on the frame immediately, because the spine is so stiff that it cannot adapt itself to the position of extension. Consequently, he is first placed in bed and urged to stay on his back as nearly continuously as possible. Several times a day he turns on one or the other side for relief from the supine position. After a few days he is placed on a frame that has a gentle curve of approximately 5 degrees. Several days later the curve of the frame is increased by 5 or 10 degrees, and every four or five days thereafter the angle of the frame is slightly increased. The change in the curve of the frame depends on the tolerance of the patient and his ability to arch his back in conformity to the convexity of the frame. In the average case, one can expect to increase the angle of the frame to 45 degrees in about from four to six weeks. There are at present two frames that are particularly useful in gradually hyperextending the spine. One is that devised and described by Dr. M. H. Herzmark.[2] His frame is adjustable as to length and width and has a joint on each side. The frame is adjusted so that the joint is opposite that part of the back where one hopes to get the greatest convexity. The curve of the frame is controlled by a turn-buckle connected by long levers to the ends of the frame. This frame is especially useful for cases of spondylitis deformans, as at first it may be made concave forward and thus make a comfortable bed for the patient with a flexed spine. Then without removing the patient, the curve of the frame may be changed slowly and as gradually as may be necessary, so that the concavity is ultimately converted into a convexity. A convexity of nearly 60 degrees may be obtained on the Herzmark frame. The other is the frame devised by Dr. Charles Rogers of Boston. It is a very ingenious apparatus. By an arrangement similar to an automobile jack, the convexity of the frame can be gradually increased without removing the patient.

During the period of active treatment on the frame, the back receives baking and massage. The patient is also encouraged to exercise his limbs and his back. Several times a day he changes to the supine posi-

2. Herzmark, Maurice H.: An Adjustable Convex Frame, J. Bone & Joint Surg. **11**:794 (Oct.) 1929.

tion, places his hands behind his back and forcibly arches his back until he can look up at the ceiling. It is surprising how much the patient can accomplish by persistent effort. The extension and ultimate hyperextension of the spine can be materially increased by judicious daily passive movement or stretching of the spine. This procedure should not be left to a masseur, who in his desire to bring improvement may use too much force and set up a painful irritation of the spine which will retard the improvement. The surgeon in charge should stretch the patient's back. He knows what he seeks to obtain by treatment, he has studied and understands the patient, and is in a position to appreciate best the degree of force and the duration of the treatment that may be safely employed to effect a correction of the deformity. When the spine can be arched backward voluntarily to a normal or nearly normal angle, one begins to move the spine laterally and in a rotatory direction.

One aims for a complete correction of the deformity. Sometimes, however, because of the severity of the disease process, a cure is impossible, and one must be content with only an improvement. The corrective measures are continued until there is no further change despite the use of strenuous force.

When a cure or the maximum improvement has been obtained, the patient is left on the frame several weeks longer to assure the permanency of the result. In the meantime, he is measured for a Taylor spinal brace. This is preferred to other spinal supports, because it fixes the shoulder and pelvic girdles while exerting corrective pressure on the dorsal area. When the brace has been applied, the patient is allowed to sit up or stand for brief periods. Gradually the period out of bed is extended until the patient is able to be about for several hours a day. He can then be discharged from the hospital and the treatment completed at the patient's home, in the physician's office or, in the case of a service patient, in the dispensary. The local treatment to the back should be kept up for many months.

During the greater part of the day the patient lies on the convex frame. When out of bed, he wears the spinal brace. He must continue with massage, stretching of the back and corrective exercises. The surgeon cannot relax his efforts until there is definite evidence over a period of many months that there is no tendency to relapse of the deformity.

REPORT CASES

Case 1.—W. L., aged 21, was admitted to the hospital on Dec. 22, 1927. His chief complaint was of pain and stiffness of the back, pain in the shoulders and weakness of the lower limbs. About two years previously he fell a distance of 15 feet, striking the ground in the sitting position. One month later he began to have pain in his back and right hip. The stiffness of his back began one year before admission to the hospital and gradually increased, so that at the end of

six months he was unable to bend sideways, forward or backward. During the last few months he tired easily and was unable to lift objects from the floor. Later he had pain in both shoulders. His past history was unimportant, except that he had had the ordinary diseases of childhood and at the age of 8, typhoid fever.

On admission to the hospital, he presented every evidence of spondylitis deformans. He was in poor general condition. He stood and walked with his body inclined forward (fig. 4). His gait was awkward. There was stiffness and loss of mobility in the dorsal and lumbar areas, with a marked increase in the dorsal curve and flatness in the lumbar region. The cervical spine was

Fig. 4 (case 1).—W. L., on admission, showing the typical attitude of a person with moderate grade of spondylitis deformans. The head is thrust forward. There is an increase in the posterior curve of the dorsal area. The lumbar region is flat.

freely movable, and neither the shoulders, hips, nor any of the other joints were involved. The x-ray pictures of the spine showed little positive change in the vertebrae. The Wassermann and gonococcus fixation tests were negative.

This patient evidently had a spondylitis deformans in which only the spinal joints were involved. The disease probably resulted from the injury sustained two years previously. There was no evidence of any infectious bacterial agent. The attack of typhoid fever, noted in the history, occurred so long ago that it probably had no relation to the spinal lesion. Although the x-ray pictures showed

no ankylosis, the spine was rigid, and the patient had a well marked flexion deformity of the trunk. This patient was at a stage in his disease when treatment could not only correct the existing deformity, but prevent future distortion of the spine. Accordingly, he was given the treatment outlined. He was kept on a convex frame for several months. The backache and the pains in the limbs disappeared, and the deformity was corrected. He was discharged wearing a Taylor spinal brace (fig. 5), with the trunk restored to the normal attitude.

CASE 2.—Max B., aged 35, was seen in February, 1928. His chief complaint was of stiffness of the back and curvature of the spine. The known duration was

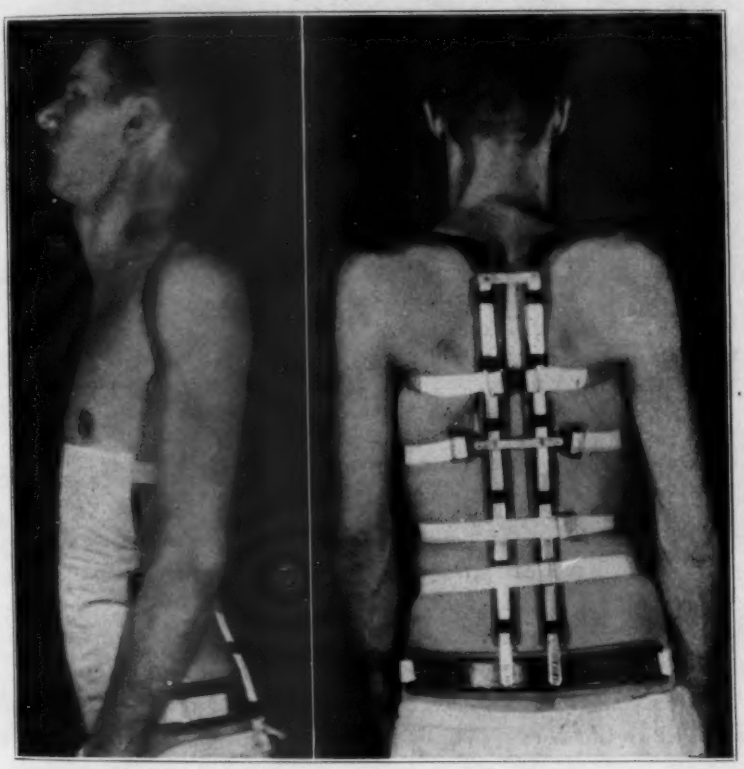


Fig. 5 (case 1).—W. L., at the end of the hospital treatment, showing correction of the deformity. He is wearing the Taylor spinal brace, which maintains the attitude of extension of the spine obtained by treatment on a convex frame.

three years. He was a tailor and had always sat with his body bent forward. His symptoms were initiated by pain across the lower part of the back. Gradually, his back became stiff.

This patient was underweight and in poor general condition. His spine was curved backward markedly in the dorsal region and was flat in the lumbar area. His trunk was fixed in flexion. There was complete immobility of the dorsal and lumbar vertebrae. In the cervical segment of the spine there was slight motion which was very painful. No other joints were affected. The x-ray pictures of the spine showed an increase in the dorsal curve and an obliteration of the lumbar lordosis. There were no osteophytes or bony bridges between any of the vertebrae.

This was a case of extreme spondylitis deformans due, probably, to many years of faulty posture. All of the vertebrae, including those in the cervical area, were affected. Since there was no bony ankylosis, as evidenced by negative x-ray pictures, the prognosis was favorable and one might expect to correct the deformity completely by the postural treatment outlined.

CASE 3.—Mrs. K. was seen by me in January, 1929. She complained of deformity of the back, pain in the right thigh and a limp on the right side. Four years previously, following the birth of her second child, she began to have backache. This gradually increased, and her back became increasingly deformed. Examination showed that she had a marked degree of spondylitis deformans. Her spine was bowed backward; her head was held forward. There was complete rigidity of the spine and loss of mobility in all of the intervertebral joints, except that between the occiput and the atlas. There was enough motion in the occipito-atloid joint to permit flexion and rotation of the head. In addition, she had marked involvement of the right hip joint. The limb was flexed to an angle of 150 degrees. There was about 40 degrees of flexion, practically no abduction, and only a few degrees of rotation. The x-ray pictures showed a very advanced osteo-arthritis of the right hip and of all of the vertebral joints. In this case the arthritic process in the spine was associated with an arthritis in the right hip.

CASE 4.—A. Y., aged 65, had pains in all of her joints for fifteen years. During the last five years she has suffered more particularly from pain in her back and in her knees. Examination showed that she had complete immobility of the dorsal and lumbar vertebrae, marked backward bowing in the dorsal area and flatness in the lumbar region. The motions in her cervical spine were limited to about half of the normal. She had a very marked degree of arthritis in both sacro-iliac joints, in both shoulders, in the fingers, in both hips and in both knees. In this case the spondylitis was part of a generalized arthritis.

The foregoing four cases were chosen as representative of the different types of spondylitis which one encounters. They have also been cited in the order of frequency with which one sees the different lesions associated with spondylitis deformans.

SUMMARY

To review briefly the preceding considerations: Spondylitis deformans is a chronic disease of the back characterized by increasing stiffness and deformity of the spine, backache, pains in the head, chest or extremities, headache and impairment of health. Although there are numerous causes of this disease, the final pathologic change is the same in all varieties. The most disabling feature of this disease is the flexion deformity of the spine. Treatment to be effective must be instituted before there is complete bony ankylosis of the spine. The deformity can be corrected, or at least reduced, by continuous treatment on a convex frame, supplemented by physiotherapy, stretching of the back and voluntary corrective exercises. Following the correction of the deformity, a favorable result can be assured only by a long period of support of the back in a spinal brace.

THE EFFECT OF ATELECTASIS ON THE PULMONARY BLOOD VOLUME*

JACOB FINE, M.D.
AND
CECIL K. DRINKER, M.D.
BOSTON

Heretofore, the methods used for measuring the effect of various types of atelectasis on the pulmonary circulation have been too indirect to justify positive assurance as to the actual quantitative variations in blood volume that occur in a lung as a result of pneumothorax or bronchial obstruction. The evidence available is adequately reviewed in the recent exhaustive article by Coryllos and Birnbaum.[1] In support of the ischemic effect of obstruction atelectasis, these authors offer further evidence by perfusion experiments of the lungs with india ink. Microscopic examination of the atelectatic lung, with the interalveolar capillaries rendered visible by this method, shows by comparison with the normal lung a marked decrease in the number of capillaries per unit of parenchyma. From this they conclude that the blood content per alveolar sac and, therefore, for the whole lung is less than for a normal lung. With Bruns,[2] who used a colorimetric method of measuring the relative amount of blood in the sound and in the collapsed lung, they agree that the decrease in blood capacity is proportionate to and "regulated by" the degree of collapse.

Since the physiologic mechanism underlying the success of modern collapse therapy is not yet clearly understood, it seems that a direct quantitative determination of the total blood and lymph flow in a collapsed lung would lead to an elucidation of the factors involved in the obviously effective measures now in use.

This report deals with a method, adapted from one published in 1923 by Drinker, Shaw and Drinker,[3] of obtaining such quantitative data as

* Submitted for publication, June 5, 1930.

* This research has been aided by a grant from the DeLamar Mobile Research Fund.

* From the Department of Physiology, Harvard School of Public Health, and the Beth Israel Hospital.

1. Coryllos, P. N., and Birnbaum, G. L.: Circulation in Compressed Atelectatic and Pneumonic Lung, Arch. Surg. **19**:1346 (Dec.) 1929.

2. Bruns, O.: Arch. f. klin. Med. **108**:469, 1912; Beitr. z. Klin. d. Tuberk. **12**:1, 1909.

3. Drinker, C. K.; Shaw, L. A., and Drinker, K. R.: J. Exper. Med. **37**:829, 1913.

far as the blood flow is concerned. They were able to quantitate accurately the amount of manganese deposited in various organs of the cat following intravenous injection of a suspension of manganese dioxide or manganese silicate particles. But it was felt that for the purposes of this study a colloidal solution of a nontoxic, insoluble, nondiffusible substance, which could be used as a perfusate and accurately quantitated, would be preferable. Colloidal nickel sulphide (solubility 0.003 mg. per liter 20 C.) was employed because Fairhall,[4] in 1926, published a reliable method for the quantitative estimation of nickel in biologic material.

The following experiments give as direct evidence as it seems possible to obtain that atelectasis, whether induced by pneumothorax or bronchial obstruction, definitely and markedly decreases the total blood volume of the affected lung.

Three series of experiments were carried out: the first, to determine the normal ratio of total blood volume of the two lungs; the second, to observe the effect of a partial or complete compression atelectasis (pneumothorax) on this ratio, and the third, to observe the effect of a total obstruction atelectasis (bronchial ligation) on this ratio. The rabbit was used for all the experiments, chiefly because of its relatively rigid and imperforate mediastinum as compared with other laboratory animals.

METHOD

All experiments were carried out under intraperitoneal barbital anesthesia.

The nickel sulphide perfusate was prepared as follows: "Nickel sulphide, C. P." (Eimer and Amend) was repeatedly washed with distilled water until all of the soluble nickel salts present were removed. An excess of this was shaken up with a liter of 5 per cent solution of purified acacia brought to a p_H of 7.4 and allowed to stand. The supernatant colloidal solution of nickel sulphide was siphoned off and used for intravenous injection. This solution is stable and runs from a buret without leaving the slightest trace of precipitate on the sides of the tube.

The first series of six rabbits were treated as follows: A cannula was inserted in the left carotid artery, and another, connected to a buret containing the perfusate, was inserted into the right jugular vein. The animal was bled, and, when about half exsanguinated, the perfusate (from 50 to 100 cc.) was slowly run into the vein until the blood from the carotid artery was practically black, soon after which the animal died. The trachea was then clamped, the chest opened, both lungs ligated in situ at the hilus, and then removed, no fluid escaping from any part of the vascular system until the lungs were cut away proximal to the site of the ligature. The entire vascular system in these rabbits seemed to contain the perfusate mixed with a small proportion of blood. There was no evidence in the lungs or other tissues that any of the nickel sulphide had entered the tissue spaces by penetrating the capillary walls. All six animals showed an even diffu-

4. Fairhall, L. T.: J. Indust. Hyg. **8**:528, 1926.

sion of the nickel sulphite throughout their lung surfaces. An uneven diffusion occurred in a number of animals not included in this series, probably because of insufficient bleeding. These were discarded as unsatisfactory and were not analyzed.

Each lung was quantitatively analyzed for metallic nickel, which was taken as a measure of the total blood volume of the lung. The results showing the normal ratio of total blood volume of right and left lungs are given in table 1.

The second series of animals were treated in the same way, but were previously subjected to pneumothorax. This was accomplished by injection of air, in amounts varying from 30 to 50 cc., into the pleural space, a water manometer being used as a guide, so that in all but two or three cases no positive intrapleural tension was present when the pneumothorax was completed. The degree of collapse resulting was not proportionate to the amount of air introduced. The reason for this is not clear, but those cases in which the air was slowly injected were usually more completely collapsed. In several animals not listed in the tables, the lung was reduced in size to far below that seen in full expiration without showing the liver-like consistency of atelectasis.

TABLE 1.—*Ratio of Total Blood Volume of Right and Left Lungs in Terms of Milligrams of Metallic Nickel*

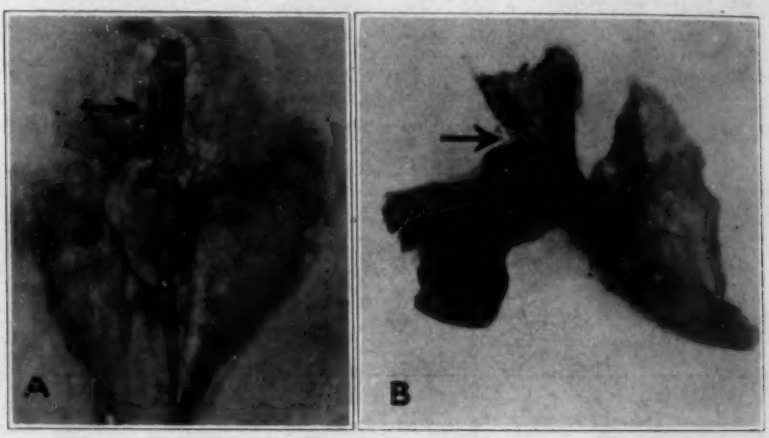
Experiment	Ratio, Mg.		Ratio, Per Cent	
	Right Lung	Left Lung	Right to Left	Left to Right
1.....	0.717	0.400	179.2	55.7
2.....	0.750	0.475	157.8	63.3
3.....	0.715	0.500	143.0	69.9
4.....	0.450	0.250	180.0	55.5
5.....	0.470	0.250	188.8	53.2
6.....	1.500	1.065	140.8	61.1
		Average	164.9	59.7

The perfusion in these animals was carried out within from ten minutes to half an hour following the induction of the pneumothorax. Following the induction, some of the animals were slightly cyanotic, some showed hyperpnea or tachypnea and others seemed to be apparently unaffected.

The third series was carried out in order to compare the effect of compression atelectasis with obstruction atelectasis. For this purpose preliminary ligation of a primary bronchus was done by way of the superior mediastinum. A tracheal cannula was connected to an artificial respiration apparatus, and the mediastinum exposed by splitting the sternum in its upper two-thirds. The thymus was lifted up from the pericardium, the aorta retracted to the left and the superior vena cava to the right, and a ligature was applied to the right primary bronchus after it was carefully isolated from all other structures. In certain cases the mediastinal pleura was not opened, but as a rule the right mediastinal pleura was unavoidably torn in lifting the thymus up and out of the way. Before the ligature was tightened, the lung was distended just enough to fill its entire pleural space, so as to avoid any compression atelectasis. In order to save the time necessary for absorption of intra-alveolar nitrogen, pure oxygen was fed into the lungs for some minutes before the ligature was applied. As soon as the ligature was applied, the chest was closed, the last ligature being tied at the height of an inspiratory stroke of the artificial respiration machine. The animal was then allowed to breathe air spontaneously, but in a few cases it was necessary to con-

tinue artificial respiration until the experiment was completed. The perfusion was carried out without much waiting, because it was noted in several preliminary experiments that not more than a few minutes were necessary to produce a total atelectasis when the lung contained pure oxygen before application of the ligature. This was not the case when air was breathed before bronchial ligation (see illustration).

Van Allen and Adams [5] have recently reported their inability to produce atelectasis in a normally breathing animal subjected to total bronchial obstruction. They consider that straining respiration is essential. The time necessary to absorb the incarcerated nitrogen seems to be the important factor. Andrus [6] obtained total atelectasis in three days, and Coryllos and Birnbaum [1] secured the same result in twenty-four hours.



Lungs removed one-half hour after ligating the right primary bronchus in the rabbit. In *A*, the animal was breathing air before ligation; result, no atelectasis; in *B*, it was breathing oxygen before ligation; result, total atelectasis. The arrows point to the ligature on the right primary bronchus.

In both the second and the third series, as in the first, no animal was used for analysis that failed to show an even diffusion of nickel sulphide throughout the lungs.

COMMENT

From table 1, it is evident that the rabbit's right lung has an average of 164.9 per cent total blood volume as compared to the left lung. The variations from this mean do not appear too excessive to make the average result far from the truth.

5. Van Allen, C. M., and Adams, W. E.: Surg. Gynec. Obst. **1**:385, 1930.

6. Andrus, W. de W.: Cardiorespiratory Physiology Following Collapse of One Lung by Bronchial Ligation, Arch. Surg. **10**:506 (Jan.) 1925.

From the upper half of table 2, it appears that a partial atelectasis of varying degree, roughly estimated by surface inspection, in the right lung reduces the normal ratio of blood volume of the right lung as compared with the left from an average of 164.9 per cent to one of 122.3 per cent—a reduction in total blood volume in the right lung of 25.9 per cent.

It is obvious that the actual amount of nickel present in the different animals varies considerably. This is due to the varying concentration of the nickel sulphide particles in the different samples of perfusate made up for injection and to the varying degrees of exsanguination in

TABLE 2.—*Effect of Partial to Complete Compression Atelectasis of the Lung on Its Total Blood Volume Measured in Terms of Milligrams of Metallic Nickel*

Lung Compressed	Experiment	Air Used for Pneumothorax, Cc.	Extent of Atelectasis Obtained	Amount of Metallic Nickel, Mg.		Ratio, Per Cent	
				In Right Lung	In Left Lung	Right to Left	Left to Right
Right	1	50	Partial (about ⅓ complete)	0.163	0.113	144.4	69.2
	2	40	Partial (about ½ to ⅔ complete)	1.250	1.000	125.0	80.0
	3	35	Partial (about ⅔ complete)	0.625	0.563	111.1	90.0
	4	35	Partial (about ¾ complete)	0.625	0.500	125.0	80.0
	5	40	Partial (about ⅓ to ½ complete)	0.900	0.700	128.5	77.7
	6	40	Partial (degree not noted)	0.750	0.750	100.0	100.0
					Average	122.3	82.8
Left	7	45	Partial (about ⅓ complete)	0.750	0.400	187.5	53.3
	8	35	Complete	0.750	0.563	133.2	75.0
	9	Undetermined *	Complete	9.750	5.000	195.0	51.2
	10	Undetermined *	Partial (about ⅔ complete)	11.880	5.020	236.6	42.2
	11	30	Complete	9.750	1.450	672.4	14.6
	12	30	Complete	7.500	0.813	923.0	10.8
					Average	391.3	41.2

* Pneumothorax induced by small opening in pleura and closed after several inspirations.

the different animals. Except for experiment 1, table 2, in which the small amounts of nickel present may, because of the greater chance of error in quantitative analysis, account for the rather wide variation from the average ratio, the results show a fairly satisfactory approximation to the average.

It is also evident that the amount of reduction in blood volume of the compressed lung bears no close relation to the extent of the atelectasis obtained. This may be due to an uneven distribution of the air in the pleural space, producing a widely distributed compression effect on the capillaries without evenly collapsing the alveoli in all directions.

In the lower half of table 2, except for experiments 7 and 8, the left lung, totally atelectatic in most cases, shows a very considerable,

but greatly varying, reduction in blood volume as compared with the right lung, as is evident from the change in the relative blood volumes of the two lungs in favor of the right lung. In experiments 7 and 8, this change has not occurred. It should be stated that in both of these animals the right lung on removal was very emphysematous, which was not the case in any of the other animals in all of the series. That this interfered with the transference of the excluded blood from the left lung into the capillaries of the right lung is possible. At least, so far as experiment 8 is concerned, in which the result is altogether at variance with the rest of the series, it should be added that the heart failed during the middle of the perfusion and may have thus interfered with the transference of the blood excluded from the left lung into the right. For it is assumed that in collapse of one lung the total pulmonary blood flow is not greatly altered unless the right ventricle fails (Dock and Harrison [7]).

Here again, as in the first six animals, the reduction in blood volume is by no means in direct proportion to the amount of atelectasis obtained, which was complete in three of the last four animals in the series. This, also, may perhaps be accounted for on the basis of varying degrees of intrapleural tension, causing different degrees of capillary compression. In one animal not included in the series, the pneumothorax compressed the left lung tightly against the spine and reduced its size to not more than one-half the volume expected in full expiration, without producing more than a few small islands of atelectasis. In spite of the absence of atelectasis, the blood content of the left lung was 0.75 mg. as compared with 3.43 mg. in the right—a decrease in the left lung of 63.4 per cent of the average normal.

The more complete atelectasis obtained in experiments 8 to 12 was probably due to the introduction of air more slowly than in experiments 1 to 6. The much greater quantities of nickel present in experiments 9 to 12, inclusive, are due to the use of a far more concentrated perfusate and possibly, to some extent, to a more complete exsanguination of the animal.

The average decrease in total blood volume of the left lung (completely atelectatic in four of six cases, experiments 7 to 12, inclusive) is 31 per cent. If, however, experiments 7 and 8 are excluded, the average decrease is 54.5 per cent. Comparison of this with a 25.9 per cent decrease in partial atelectasis of the right lung gives evidence in favor of the contention of Bruns [2] that the reduction in blood volume of the lung is directly dependent on the degree of atelectasis.

---

7. Dock, W., and Harrison, T. R.: Am. Rev. Tuberc. **10**:534, 1924-1925.

Dock and Harrison [7] agreed with Cloetta [8] that hyperemia is found immediately following collapse, on the basis of their observation that from 52 to 58 per cent of the total pulmonary blood volume flows through the collapsed right lung during the first few hours following induction of pneumothorax. They stated that it takes a longer time than this for the lung to become atelectatic. In our experiments, the interval between the induction of pneumothorax and the removal of the atelectatic lung after perfusion did not exceed thirty minutes and often was much less, so that their defense of Cloetta's observation cannot be sustained. The normal blood volume of the right lung in their experiments may have actually been more than from 52 to 58 per cent of the total, so that in fact these figures may represent a reduction in the blood volume of the collapsed right lung.

TABLE 3.—*Effect of Absorption Atelectasis on Total Blood Volume of Affected Lung in Terms of Milligrams of Metallic Nickel*

Experiment	Primary Bronchus Ligated	Amount of Metallic Nickel, Mg.		Ratio, Per Cent	
		In Right Lung	In Left Lung	Right to Left	Left to Right
1.....	Right	0.375	0.563	66.6	150.0
2.....	Right	0.438	0.750	58.3	172.0
3.....	Right	1.500	1.500	100.0	100.0
4.....	Right	1.375	1.750	78.5	127.2
5.....	Right	1.188	1.500	79.1	126.3
6.....	Right	1.000	1.125	80.0	112.5
7.....	Right	1.125	0.750	150.0	66.6
			Average	87.5	122.1

The conclusions of Corper, Simon and Rensch,[9] to the effect that no decrease in circulation occurs shortly after collapse, are likewise not supported by the results shown in table 2.

These observations, along with the microscopic evidence offered by Coryllos and Birnbaum, agree with Gardner's [10] pathologic studies on human lungs to the effect that pneumothorax produces a compression of the capillary bed.

The third series of experiments, summarized in table 3, deal with absorption atelectasis. It was thought desirable to compare the effect of absorption obstruction atelectasis with compression atelectasis, in order to eliminate the factor of capillary compression by extrapulmonary pressure.

In seven experiments, detailed in table 3, the totally atelectatic right lung showed a total blood volume which was only 87.5 per cent of the

8. Cloetta, M.: Arch. f. exper. Path. u. Pharmakol. **66**:409, 1911.

9. Corper, H. J.; Simon, S., and Rensch, O. B.: Am. Rev. Tuberc. **4**:592, 1920.

10. Gardner, L. U.: Am. Rev. Tuberc. **10**:510, 1924-1925.

left, a reduction from the normal blood volume of 46.9 per cent. The seventh experiment in the series gives a result that is only explainable as an error, probably in the chemical analysis.

SUMMARY

It appears, therefore, that partial to complete atelectasis induced by pneumothorax at once reduces the total blood volume of the affected lung by amounts varying, on an average, between 25.9 to 54.5 per cent, and in individual cases by a considerably higher percentage. Absorption atelectasis reduces the total blood volume of the affected lung by 46.9 per cent.

In the former type of atelectasis the reduction is not dependent only on the actual amount of atelectasis obtained. An additional factor is the amount of compression induced. Thus, in no case of total absorption atelectasis was there such a large reduction as was obtained in experiments 11 and 12 (75.6 and 82 per cent, respectively), table 2, of the compression atelectasis series. Hence, the actual reduction probably depends on the variable factor of intrapleural tension in addition to the atelectasis per se. Although the extent of the atelectasis obtained is not necessarily proportional to the amount of compression, nevertheless, the reduction in blood volume is, in general, greatest when the atelectasis is complete.

Whether the reduction in blood volume in either type of collapse, aside from the added effect of the extrapulmonary compression of the capillaries in the pneumothorax type, is due to the shrinkage of the capillaries purely because of alveolar collapse or to some other factor will be the subject of the next report. In the experiments made to ascertain this, the technic here described will be used.

CONCLUSIONS

1. A reliable chemical method for the quantification of the relative blood volumes of the two lungs in the rabbit is outlined.

2. This method shows that the rabbit's right lung has a much greater blood volume than the left lung.

3. Absorption atelectasis at once reduces the total blood volume of the affected lung to a considerable degree.

4. Compression atelectasis also at once markedly reduces the total blood volume of the affected lung, in a number of instances to an extent far greater than is obtained in absorption atelectasis.

A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.
LOS ANGELES
E. STARR JUDD, M.D.
ROCHESTER, MINN.
LINWOOD D. KEYSER, M.D.
ROANOKE, VA.
GORDON S. FOULDS, M.D.
TORONTO, CANADA
JEAN VERBRUGGE, M.D.
ANTWERP, BELGIUM
AND
ADOLPH A. KUTZMANN, M.D.
LOS ANGELES

KIDNEY

Calculi.—Ainsworth-Davis [1] reported a case of renal calculus associated with solitary cyst of the left kidney. A man, aged 54, was seen two hours after the beginning of a typical attack of renal and ureteral colic. From four to six years before, he had had attacks of pain in the lower left side of the abdomen, which occurred suddenly and generally lasted from six to seven hours. He had been free from attacks for the preceding two years. Hematuria was noted during a less severe attack.

Cystoscopic examination disclosed mild cystitis and slight swelling of the left ureteral orifice. A catheter was passed to the pelvis of the left kidney. Resistance was noted at the ureteropelvic juncture and about 7.5 cm. lower. As soon as the catheter reached the pelvis of the kidney, a flow of urine was established and the renal colic subsided. The roentgenogram did not obtain a shadow indicating a stone in the left kidney or ureter. There was displacement of the renal shadow upward by a spherical body about 10 cm. in diameter, which was probably attached to the lower pole of the kidney and moved with it on respiration; this body displaced the lower part of the ureter inward and forward, causing marked kinking. At operation a stone about 1.9 cm. long and 1.2 cm. wide was found in the renal pelvis. The lower half was replaced by a solitary cyst.

The pain subsided immediately on relief of distention of the renal pelvis, but no relationship was found between the occurrence of the stone

1. Ainsworth-Davis, J. C.: Renal Calculus Associated with a Solitary Cyst of the Left Kidney, Brit. M. J. **1**:10 (Jan. 4) 1930.

and the cyst. Ainsworth-Davis stated that in the case of doubtful renal swelling, exploration should always be done, as an exact diagnosis was impossible in some cases. Renal tumors may reach a considerable size without being palpable if the patient is fat.

Pedroso [2] performed nephrectomy for tuberculosis and found the renal pelvis filled with soft calculi. Calculi composed of bacteria and fibrin of the urinary tract have rarely been observed. The first observation was made by Marcet in 1817 or 1818; since then 25 cases have been reported. As this condition does not produce special symptoms, the diagnosis has never been made prior to operation; in the majority of cases, calculi have been discovered in operations for other conditions. These calculi, as in the case of hard calculi, may be found in any part of the urinary tract. In most cases reported, they have been present in the kidney, and in a few cases in the bladder. As many as 100 concretions have been found in the kidney by Gage and Beal; 70 were found in Pedroso's case. Fewer are found in the bladder, generally two or three, and they are usually larger. Those of the kidney vary from 1 to 4 cm. in diameter; when numerous they are faceted and have the appearance of gallstones. The color depends on their composition; when they are formed of concentric layers of fibrin and albumin they are yellowish or grayish white; those whose interior is of a granular or pulpy dark-brown substance are brownish white, the color of the contents showing through the capsule. Their consistence is that of wax or of a baked bean; they are elastic and slight pressure crushes them. Examination of the calculi has shown that they are composed of albumin, fibrin, amyloid substances and many bacteria. These albuminous substances form concentric layers like the layers of an onion, among which bacterial masses are grouped; in other cases the nucleus is formed by bacterial masses or by mucous filaments. These calculi are formed in the kidneys in pyelitis or pyonephrosis by bacterial nuclei which grow in the periphery and gradually increase in size, by blood clots or necrotic filaments loosened from the renal pelvis in cases of pyelitis, or by pus in pyonephrosis. These coagulations constitute a nutritive medium for bacteria, and after having been largely absorbed by them, constitute the albuminous framework of the calculi.

This condition does not cause peculiar symptoms; patients suffering from it complain of symptoms similar to those of renal lithiasis with its complications. The treatment in cases in which there is parenchymatous destruction or pyonephrosis is nephrectomy; if a preoperative diagnosis can be made and there is no parenchymatous destruction, pyelotomy may permit the extraction of the calculi without removal of the kidney.

---

2. Pedroso, Gonzalo: Albumin and Fibrin Calculi of the Kidney, J. Urol. **23**:627 (June) 1930.

Koll [3] stated that multiple calculi in any part of the kidney, as well as pelvic stones, should be removed. When a single small calculus in a calix is not producing any symptoms it should be left alone. If bilateral calculi are removed, sufficient time for complete convalescence should elapse before the second kidney is operated on. If the opposite ureter contains a concretion, the ureteral calculus should be permitted to pass either spontaneously or by the aid of oil before the renal stones are removed. If there is doubt as to the advisability of nephrectomy, the kidney should be given a chance to recover, as it can always be removed later. Koll does not believe in pyelotomy as a routine procedure. Combined pyelonephrotomy or nephrotomy alone often is productive of less trauma and less permanent ill results. Ninety-eight per cent of calculi that have entered the ureter will pass either spontaneously or with the aid of instrumentation. Cutting into a ureter is not advocated, as stricture results in most instances, necessitating nephrectomy.

Bugbee [4] considered the large, branching type of calculus and the possibility of its remaining in place for a long time, without causing symptoms and not being detected until infection takes place. If watched for a period of years these stones seem to change little and the patients get on fairly comfortably. He cited one instance in which a roentgenogram revealed a stone of this type. After three years the roentgenogram showed that the same calculi were present and were the same size as in the previous roentgenogram. The patient is leading an active life and apparently is in good health.

Pennock [5] considered the type of microscopic stone that is responsible for hematuria. These cases of essential hematuria have presented an enigmatic problem. Bauer was able to demonstrate small calculi in many cases after much difficulty and the study of numerous sections. He demonstrated minute calculi which he believed were the etiologic factor in a case regarded as essential hematuria in which the kidney was removed because of persisting bleeding which produced secondary anemia. The kidney was apparently normal. Repeated sections gave normal results. One hundred twenty-five sections of the kidney were made before microscopic calculi were found which were believed to be the etiologic factor in the hematuria. He later proved the presence of calculi in several other cases.

Cysts.—Hepler [6] stated that large, usually solitary, cysts of the kidney are acquired. They are not a distinct entity with a common

3. Koll, I. S.: Conservatism in Urology, J. Urol. **23**:581 (May) 1930.

4. Bugbee, H. G., in discussion of Lewis, B., and Grayson, C.: J. Urol. **23**:13 (Jan.) 1930.

5. Pennock, W. J., in discussion of Lewis and Grayson (footnote 4).

6. Hepler, A. B.: Solitary Cysts of the Kidney, Surg. Gynec. Obst. **50**:668 (April) 1930.

etiology. Recognized pathologic conditions of the kidney cause them, but only when so situated as to produce a combination of group tubular obstruction and anemic degeneration of the parenchyma from circulatory disturbances in the same segment of the kidney. In some instances an additional factor is repeated, prolonged hemorrhages into the same area. This conception explains the variation in size, number, contents, wall of the cyst and associated renal conditions on the basis of variation of the direct etiologic factor, the amount of group tubular obstruction and the area of nutritional disturbance depending on the size and distribution of the vessels involved. Among the clinical and pathologic features of large renal cysts which lend support to this hypothesis are:

1. The average age of 45 years, a period when vascular lesions, such as arteriosclerosis, endarteritis, aneurysms, infarcts and acquired lesions, such as tumor, are common.

2. The rather frequent association of these cysts with lesions which might produce the conditions assumed to be necessary for their formation.

3. The presence of groups of atrophied glomeruli and tubules in the wall of the sac, indicating its origin from renal parenchyma which has undergone compression atrophy with substitution by connective tissue.

4. The presence of remnants of neoplasm in the walls of many of the hemorrhagic cysts as the only indication that a tumor was concerned with their formation.

Finally, by creating experimentally the conditions assumed to be necessary for the formation of cysts, Hepler stated that he was able to reproduce a large solitary cyst similar in every detail to those found in the kidney of man.

Grove [7] stated that in most of the reported cases of solitary serous cysts of the kidney, urinary symptoms, if present, were slight. Attention is drawn to the genito-urinary tract by the presence of a palpable mass in the abdomen, or as a result of exclusion of the kidney as a source of the lesion. As these cysts do not communicate with the calices or renal pelvis, pyelograms usually do not show distortion of the pelvis unless the cyst is large enough to bulge into it. If the cyst is at the upper pole, it may, by its weight, push the kidney down, producing ectopia. Displacement of the kidney may produce various deformities of the ureter which may cause symptoms referable to the urinary tract.

Grove reported a case of solitary cyst of the kidney which was large enough to produce symptoms of pressure referable to the gastro-intestinal tract. Functional and cystoscopic studies did not reveal anything abnormal. Although the cyst was large, it was possible to perform a partial resection and save a large portion of a normally functioning kidney. Such tumors are not uncommon, as noted by pathologists.

7. Grove, J. S.: Solitary Serous Cysts of the Kidney, J. Urol. **23**:661 (June) 1930.

Polycystic disease of the kidney is extremely uncommon in children. Wakeley [8] noted the rarity of unilateral occurrence. He reported the case of a boy, aged 20 months, seen on April 6, 1929, with a large abdominal tumor, which was first noticed by the child's mother a few months after birth. The child was the third of the family; the other children were normal. Examination revealed a large, smooth tumor which occupied the whole right side of the abdomen and extended up toward the margin of the liver and across the median line. The tumor was firm and felt like rubber. The urine was normal except for a few erythrocytes and pus cells. Renal function was normal. Nephrectomy was performed on April 22 through an anterior incision, with removal of the large tumor. The opposite kidney was examined and found to be apparently normal. Convalescence was uneventful; the child gained rapidly and left the hospital on May 5. When he was last examined the disease had not developed in the opposite side.

The tumor measured about 18 by 12 cm. and weighed 1.6 Kg. It was reniform with definite cystic dilatations on its surface. The pelvis of the kidney was definitely dilated. On section, normal renal tissue could not be seen. The kidney contained numerous cystic spaces varying considerably in size. Some of these spaces contained fluid; others contained a colloid substance. The structure of the kidney had been completely replaced by the cysts. The type of epithelium lining the cysts showed considerable variation; in some it was definitely columnar, with large vesicular nuclei situated toward the base of the cells. In other cysts, including the smallest, the epithelium was flattened and the cells resembled endothelial cells. All intermediate types of cell were present. In all cysts the epithelium was only as thick as a single cell. The stroma was loose and fibrous, showing areas of hyaline degeneration. Hemorrhage, mostly recent, had occurred. Some pigment was present, chiefly within phagocytes. The stroma also showed areas of infiltration with inflammatory cells, including large numbers of plasma cells.

Hydatid Disease.—Lee-Brown [9] stated that the diagnosis of a renal hydatid depends on the physical signs and symptoms, the chief of which is the presence of tumor. If the cysts rupture, with absorption of a considerable amount of antigen, general symptoms of hydatid anaphylaxis may be present. The condition of the urine depends on whether the hydatid is open or closed. In the closed variety, hematuria may occur only occasionally. In the open type, with infection superimposed, hooklets, scolices, small daughter cysts and pieces of laminated membrane may be found. Pyelographic evidence is of special significance.

8. Wakeley, C. P. G.: A Case of Unilateral Polycystic Kidney in a Child, Brit. J. Surg. **18**:162 (July) 1930.

9. Lee-Brown, R. K.: Renal Hydatid Disease, J. Urol. **23**:611 (June) 1930.

In long-standing cases deposition of lime salts often occurs in the thickened adventitia. This deposit of calcium renders the adventitia impervious to roentgen rays and casts a characteristic shadow. Such calcification occurs only occasionally and cannot be expected in every case. Roentgenograms do not offer much diagnostic aid early in the disease, but the pyelogram, except in a small percentage of cases, supplies evidence, depending on whether the hydatid is open or closed. In the event of closed hydatid, the evidence produced will be similar to that of a localized tumor obliterating a portion of the pelvis.

The treatment for hydatid disease in general is essentially surgical. There is no direct blood supply to a hydatid cyst and it depends entirely on osmosis for its nutrition. The earliest surgical treatment was the aspiration method, consisting of the introduction of a hollow needle into the cyst and withdrawal of the fluid. By this method it was hoped that collapse of the cyst would occur and be followed by fibrous degeneration. The operation failed to produce the desired results, and complications frequently resulted which called for more radical measures. Puncture of the cyst often permitted escape of hydatid fluid into the surrounding tissues, and in this way scolices escaped and later developed into secondary daughter cysts. If much fluid escaped there was grave danger that anaphylactic shock might result. Infection often resulted from puncture of the cyst in spite of rigid aseptic technic, and frequently incision and drainage were necessary. The surgical measures now employed depend on whether the disease is confined entirely to the kidney or whether it extends beyond the kidney into the adjoining tissues. Nephrectomy is the operation of choice in all cases of renal hydatid and in the majority of "closed" cases. There are two exceptions to nephrectomy in closed cases of hydatid disease: (1) if the cyst is small and confined to one pole of the kidney, partial nephrectomy might be considered, and (2) if the cyst is calcified, which means activity has ceased, and the remaining renal tissue is worth conserving, there is no object in surgical removal. If there is one large simple and adherent mother cyst, in which gross infection is not present, it is exposed through the loin and after careful packing off, a trocar attached to a suction apparatus is introduced and the fluid content withdrawn. Following this, alcohol or a solution of formaldehyde (10 per cent) is introduced, slightly less in quantity than the amount of hydatid fluid withdrawn. This is left in place for three or four minutes in order to devitalize the parasite. The alcohol or formaldehyde is then withdrawn, the cyst is incised and the content, consisting of daughter cysts, laminated membrane, brood capsules and débris, is removed. The cyst having been completely emptied, the interior is swabbed out with alcohol, the cyst is closed with catgut sutures and the collapsed wall is sewed to the deep aspect of the lumbar incision. A rubber tissue drain is introduced down to, but not into, the cyst and the

wound is closed in the ordinary way. The rubber tissue drain is employed because of the effusion that invariably follows evacuation of the cyst.

Ectopy.—Campbell [10] reported a series of 27 cases of renal ectopy observed in 13,000 postmortem examinations, with a brief consideration of the anatomico-clinical features of ectopy. The condition occurred once in about 660 cases. The anomaly is sufficiently common and is so potentially serious clinically as to warrant grave consideration. The technical difficulties of surgical intervention are usually extreme in the treatment of low ectopic kidneys, and are due not only to the site of the organ but to the congenitally short ureter and short, anomalous vascular supply. If a seriously diseased kidney is low in the pelvis and the remaining kidney is functionally competent, nephrectomy is the treatment indicated since it is anatomically difficult or impossible to accomplish extraperitoneal drainage of these organs, and transperitoneal drainage usually results in peritonitis. In none of Campbell's series was renal ectopy a direct cause of death.

[ED. NOTE.—Campbell, in 1929, reviewed fifty-five cases of rupture of the bladder from the Bellevue Hospital. His conclusions in general agree with those of de Tarnowsky. The diagnosis of rupture of the bladder is not always simple. Shock is common. Pain in the lower part of the abdomen, withdrawal of a variable amount of blood-stained urine by catheter (often more confusing than helpful), cystoscopy, pneumoroentgenography or air cystography may help in diagnosis. A history of trauma with an overdistended bladder and the inability of the patient to void, except in small amount at times and with strangury, are salient features in the picture. Evidence of peritonitis or peritoneal irritation when the rupture is intraperitoneal and the finding of prevesical, perivesical, perirectal or subcutaneous urinary extravasation in the abdominal wall or perineum are of diagnostic import. From a survey of case reports it is easy to understand why it is often difficult to avoid delay in proper surgical treatment.

Rupture of the bladder is almost always associated with trauma; it is a frequent occurrence with alcoholism, at times with preexisting vesical disease, but probably is rare with simple distention. The condition is often accompanied by other traumatic lesions, such as rupture of the spleen, liver or kidneys, or by fracture of the pelvis.

Immediate operation is indicated. If possible, the rupture should be exposed and sutured. Campbell advised suprapubic drainage of the bladder with a large rubber tube. Prevesical or culdesac drainage or the use of the catheter à demeure, as recommended by de Tarnowsky, are considered by Campbell as inferior to suprapubic cystostomy. The

10. Campbell, M. F.: Renal Ectopy, J. Urol. **24**:187 (Aug.) 1930.

condition is to be regarded as an emergency, as each hour of delay brings a risk of increased mortality. Twenty of the fifty-five patients reported by Campbell as having recovered were all operated on. Both authors urged that when the diagnosis of vesical rupture is established or strongly suspected, abdominal exploration be made as an emergency procedure.]

Deming[11] studied fifty-five cases of nephroptosis. The excursion of the kidneys varied from 4 to 12 cm., the average being 5.5 cm. In 51 per cent of the cases ptosis occurred in the right kidney, in 11 per cent in the left kidney and in 19 per cent it was bilateral; in 7 per cent of the cases general visceroptosis was present. Twenty per cent of the kidneys were rotated through one or more planes up to 180 degrees. This observation, Deming stated, is important in correcting the position of the kidney at operation. The function of the ptotic kidney is rarely modified. Thirty-three per cent of the kidneys were infected with *Bacillus coli;* most of the pelves which were infected had a slight increase in capacity, although only 7 per cent had more than 20 cc.; 66 per cent had a normal pelvic capacity. In all of the cases kink, stricture or tortuosity of the ureter was present; in 80 per cent kinks were found, in 50 per cent tortuosity and in 13 per cent stricture. Deming noted the symptoms of the ptotic kidney as mainly pain, acute and chronic, due mostly to obstruction of the ureter.

In performing nephropexy, Deming begins the incision high in the costovertebral angle, continuing it downward and transversely across, halfway between the lower rib and crest of the ilium, incising portions of the external and internal oblique muscles in most cases. Approach to the kidney is made through the triangle of Petit. The fatty capsule is opened, and the kidney which is usually low-lying is easily recognized. The hand is inserted under the liver to the diaphragm. The kidney can then be replaced sufficiently high to remove all kinks and most of the tortuosities of the ureter. A series of interrupted chromic mattress sutures no. 0 are then placed through the perirenal fascia and peritoneum to the quadratus muscle. From five to eight sutures are necessary to close this aperture; they form a basket-sling for the kidney so that it is impossible for the organ to descend. This row of sutures is now enforced by bringing up all the extraperitoneal fat and suturing it with two or three mattress sutures to the quadratus muscle below the other line of sutures. The patient is kept flat in bed for sixteen days, allowed out of bed on the eighteenth day and home on the twenty-first or twenty-second day. None of the patients had complications and all but one were completely relieved of the symptoms.

11. Deming, C. L.: Nephroptosis: Its Relation to the Liver, Spleen, Stomach and Its Correction by Means of a New Operation, Am. J. Surg. **9**:218 (Aug.) 1930.

Hydronephrosis.—Legueu and Fey[12] stated that distention of the renal cavities, the characteristic lesion of hydronephrosis, is the result of two agents, dilatation and retention. Dilatation is an anatomic lesion of a static and steady nature. Retention is a physicopathologic lesion and arises from poorly performed functions of the pyelo-ureteral muscle. Although an evident anatomic lesion is found, one must make certain, before admitting its pathogenic action, that it is a first cause of retention and not a secondary deformation connected with the developments of the dilatation. Certain aspects of pyelography and ureterography favor the mechanical theory. It is necessary to ascertain definitely that these deformations are permanent and do not correspond to normal and physiologic contractions. Observation by pyeloscopy in the majority of cases demonstrates that there is neither arrest nor delay of the evacuation of the opaque medium. Hydronephrosis from mechanical reasons seems uncommon and can hardly be accepted except in cases in which catheterization is impossible. The congenital theory would be a structural abnormality, incompetence of the pyelo-ureteral muscle. There are some unquestionable cases of hydronephrosis, those in which the renal apparatus discloses morphologic malformation, but it is difficult to place in this group the majority of cases of pelvic retention. The existence of functional retention is proved by the many cases in which there is retention without any congenital lesion or mechanical obstacle. Such is the case with slight hydronephrosis characterized by retention without dilatation. This functional retention is connected with impaired action of the excretory apparatus, the variations of which can be studied by physiology and pyeloscopy. Certain experimental and clinical operative facts tend to substantiate this theory. Excretion is assured by the functional synergy of several muscular actions, which are pelvic contractions culminating in the formation of a bulb, a pyelo-ureteral sphincter action that controls the filling and evacuation of the ureter, peristaltic contraction of the ureter, a ureterovesical sphincter action that protects the ureter against the back pressure in the bladder during urination.

Clinical diagnosis depends on the character of renal pain. The most typical pain is renal colic connected with a spasm of the pelvic musculature entailing a crisis of acute retention. The diagnosis can be made only after complete roentgenologic examination.

Operative treatment is based on the pain, on the presence of infection, on the dilatation and on the degree of chronic retention. If operation is decided on, some improvement is obtained by catheterization of the ureter. If operation is performed, Legueu and Fey carefully look for causes that provoke the phenomena of excitation and inhibition

12. Legueu, F., and Fey, B.: Hydronephrosis, Brit. J. Urol. **2**:131 (June) 1930.

disturbing excretion. Nephrectomy is performed exceptionally, keeping in mind the volume of the sac, its infection, the condition of the remaining parenchyma, and the tonicity and activity of the calices and ureter which are explored in the course of the intervention. In other cases two eventualities occur: If it is possible to determine the lesion causing the retention, this cause is removed, no complementary procedures being used; if it is not possible to determine the cause of the retention, nephropexy, renal intervention or temporary nephrostomy is performed.

Eisendrath [13] reported a case in which the obstruction of the renal pelvis was due to the lower of 2 main renal arteries. Although cases of obstruction of the renal pelvis by branches of a main renal artery have been reported, Eisendrath's case is the first to be reported of obstruction by 1 of 2 main renal arteries. He advised against ligation of a polar artery, because of the danger of necrosis of the area supplied by such a vessel, the same being true of ligation of 1 of 2 main renal arteries. The frequency of the variations of the renal vessels which are of clinical importance was reviewed. Lower polar arteries from the aorta were found in 5 per cent of 1,337 kidneys, and 2 main renal arteries were found in 11.2 per cent of 1,319 kidneys by various observers. Abnormal mobility of the kidney, as pointed out by Mathé, plays the most important part in favoring obstruction by a polar artery or by 1 of 2 main renal arteries.

Walters [14] stated that the causes of hydronephrosis consist for the most part of anomalous blood vessels, usually an artery and a vein, which cross and change the angle of ureteropelvic drainage, with the possible interference of ureteral peristalsis by pulsation. Unless search is made for these vessels as they cross the ureteropelvic juncture, they are easily overlooked. With these vessels, it is usually found that angulation of the ureter at the ureteropelvic juncture by the renal pelvis or perirenal pelvic connective tissue has occurred which, with dilatation of the renal pelvis, produces ureteral compression. In some cases the absence of demonstrable obstruction in the presence of large hydronephrotic sacs suggests disturbances of neuromuscular control of the renal pelvis and upper part of the ureter. If an anomalous vessel is compressing the ureter at the ureteropelvic juncture, thus changing its course and interfering with proper emptying of the pelvis, and if the additional blood supply is sufficient, the anomalous vessel should be divided. If, however, as a result of this type of obstruction, the extrarenal pelvis is considerably dilated, it is resected to within 1.5 cm. of

13. Eisendrath, D. N.: Hydronephrosis Due to Obstruction of the Renal Pelvis by One of Two Main Renal Arteries, J. Urol. **24**:173 (Aug.) 1930.

14. Walters, Waltman: Resection of the Renal Pelvis for Hydronephrosis: Its Complications and Results, Surg. Gynec. Obst. **51**:711 (Nov.) 1930.

the renal substance, leaving the ureter attached to its dependent portion. Closure of this opening in the pelvis removes the hydronephrotic sac and changes the course of the ureter, and its opening becomes dependent. In the cases in which this was done, nephropexy was also performed to prevent further ureteral angulation. In some cases temporary nephrostomy was done also, to relieve pressure on the suture line. If for any reason there is a question of inadequate blood supply from the remaining vessels to the kidney, circulation in the anomalous vessels should not be obstructed, particularly if the opposite kidney shows any abnormality of function. Such obstruction existed in one case in which there was a large hydronephrotic sac on both sides. In such cases the dilated extrarenal pelvis is resected, or the ureter is reimplanted into the dependent portion of the pelvis away from the anomalous vessels. In several cases of hydronephrosis in which nephrectomy was necessary because the kidney was largely destroyed, compression angulation and obstruction of the ureteropelvic juncture occurred as a result of a dense sheath of connective tissue.

Resection of the hydronephrotic renal pelvis was done in one case in which there was no demonstrable cause for the obstruction. The dilated portion of the left hydronephrotic pelvis was excised and the ureter was severed from the pelvis and reimplanted into its dependent portion. Removal of the ureter from its lateral attachment to the hydronephrotic renal pelvis and its reinsertion by suture to the dependent portion of the pelvis away from these anomalous vessels is indicated if the anomalous vessels crossing the ureteropelvic juncture are of such size and importance that their division and ligation seem inadvisable.

Walters expressed the opinion that postoperative complications center around: (1) leakage of urine at the point of anastomosis with perirenal accumulation; (2) retention of urine in the kidney, leading to pyelonephritis or cortical abscesses in the kidney, and (3) ureteral obstruction at or below the pelvic incision with a persisting urinary fistula from the pelvic anastomosis. In eleven cases of hydronephrosis, resection of the renal pelvis was performed. In eight cases (nine resections) the results of operation were excellent. In four of these cases hydronephrosis was bilateral, and the renal pelvis was large and infected. Bilateral resection was performed in one case. In three additional cases of bilateral hydronephrosis successful resection of one hydronephrotic renal pelvis was performed. In three cases in which resection of the renal pelvis was performed, secondary nephrectomy was required, due to (1) persistent urinary fistula from occlusion of the ureter by postoperative infection around the ureter, and (2) pyelonephritis with cortical abscesses in two cases in which urine was being transmitted successfully from the resected renal pelvis to the bladder through the ureter. Complete recovery followed nephrectomy.

Covisa [15] divided hydronephrosis into two main groups: that due to causes of a mechanical nature and that due to causes of a dynamic nature. Among the causes of a mechanical order are included all organic lesions, congenital or acquired, such as tumors, inflammatory processes, foreign bodies, narrowness, bends and valvular formations which, acting either from inside or from outside of any part of the urinary tract, place difficulties in the way of normal excretion of urine. Under dynamic hydronephrosis may be grouped all cases in which no appreciable organic cause exists to which the development of hydronephrosis can be attributed. Its causes are sometimes processes of a toxic infection, of inflammatory infiltration of the walls of the ureter, or of disturbances of the nervous system. Modern pyeloscopic explorations and the experimental work of many investigators have demonstrated that peristalsis of the pelvi-ureteral muscle can be modified by motor disturbance and by disturbance of tonus. Motor disturbances can be excessive or defective. If excessive, they produce a hyperkinetic syndrome characterized pyeloscopically by a more rapid emptying of the pelvis than normal. They give rise to an incomplete retention syndrome, which is revealed pyeloscopically by retarded evacuation. These motor changes are manifested clinically by painful spasmodic crises, and are characterized by the absence of dilatation of the pelvis.

The treatment for hydronephrosis can be either radical or conservative. The radical treatment is nephrectomy; the conservative is nephrostomy, pyelotomy, nephropexy, denervation of the renal pedicle, cutting of the aberrant vessels and various plastic operations. Whenever conservative treatment is possible, it should be used. In many cases conservative plastic operations should be combined to bring about a more perfect therapeutic action; in all cases complementary nephropexy should be practiced to correct the mobility of the kidney, caused by the measures employed for isolating and bringing it to the surface.

[Ed. Note.—The present tendency of urologic surgeons is to employ the most conservative methods in the treatment for renal lesions whenever such measures are compatible with satisfactory results. It is now possible to utilize the less radical procedures, with the consequent saving of functioning renal tissue, sufficient in some instances to support life. These procedures are especially applicable in lesions such as bilateral hydronephrosis. White, in a study of hydronephrosis, found that the commonest form of the disease was that in which the dilatation of the kidneys began at the ureteropelvic juncture. In a large proportion of his cases, which were identified in early life and which were undoubtedly congenital, the disease was bilateral. Usually the first manifestations

15. Covisa, I. S.: Etiology and Treatment of Hydronephrosis, Brit. J. Urol. 2:133 (June) 1930.

are in adult life. The earliest cases show narrowing of the ureter from chronic inflammation, which appears to be the cause of the dilatation. In all cases pyelitis and moderate chronic interstitial nephritis are associated. Papin stated that in the surgical treatment for hydronephrosis two extremes should be avoided: the essentially surgical and the radical. Nephropexy serves satisfactorily if the ureter is kinked, and is unsatisfactory in cases in which small congenital dilatations are present. Mercier concluded from his experience with the etiology and treatment of hydronephrosis that most cases are produced by pelvic or ureteral membranes and by lowering of the kidney from 1 to 2 cm. from some undetermined cause. He stated his belief that nephropexy is the logical operation for some types of hydronephrosis because it reestablishes the normal position of the pelvis toward the ureter. Marion obtained good results in treating a number of patients for hydronephrosis by liberating the ureter at its superior position and fixing the kidney as high as possible. He stated that some cases are not due to narrowing of the ureter, but to extreme fixity to the surrounding cellular tissue and to slight ptosis of the kidney.]

Pyelovenous Backflow.—Fuchs [16] reported on pyelovenous backflow. If one injects fluid into the ureter of a human being or into the kidney of an animal after removal, the fluid often flows out by way of the renal veins, because of a direct connection between the vascular system and the upper portion of the renal pelvis. An attempt to establish the practical significance of this phenomenon has been made through animal experiments. The exact part that the pyelovenous backflow plays in pathologic changes in man is the specific object of Fuchs' paper.

A short survey of the literature, from the first observations of Gidon (1856) up to the present was given. Some of the more important points regarding pyelovenous backflow given by different authors were considered. Among these were:

1. The fate of fluid forced under pressure into the renal pelvis through the ureter. Experimental evidence has shown that such fluid is found in all tissue elements of the kidneys, chiefly in the lymph spaces and blood vessels, especially in the veins, and least in the uriniferous tubules.

2. The mechanism of the passage of fluid from the renal pelvis into the veins, as well as into the lymph vessels and uriniferous tubules. Summing up the experimental and anatomic data, it may be said that pyelovenous backflow is accomplished by direct communication between the pelvis and the venous system, initiated by rupture of the renal pelvis.

3. The pressure necessary to produce pyelovenous backflow. According to all investigators this pressure is exceptionally small. No difference was found in the required pressure of kidneys of cadaverous and living animals.

16. Fuchs, Felix: Pyelovenöser Reflux und Hydronephrose, Deutsche Ztschr. f. Chir. **224**:353 (June) 1930.

Fuchs also reviewed his investigations on the kidneys of human cadavers. Notwithstanding certain well recognized differences between the intrarenal topography of the kidneys of mammals and of man, there are significant analogies in the pyelovascular mechanism. The place of pyelovenous backflow is at the apex of a minor calix, called the fornix calices in the kidney of man. Fuchs has shown by means of a macerated preparation the relation between the fornix calices and the venous plexus of the renal sinus. He found three fourths of the circumference of the fornix calices often surrounded by a venous plexus. It is thus clear that the venous circulation in the calix must sustain considerable injury in the event of expansion of the calix. The renal pelvis is regarded as the strongest ductile segment of the upper urinary passages, whereas the parenchyma of the kidney lacks extensive ductility. It is apparent that the line of separation between the weak and strong parts of the pelvic cavity is at the point of insertion of the calix in the parenchyma of the kidney, namely, at the fornix calices. This is the place of predilection for rupture in internal pressure. For the purpose of observing the conditions of rupture of the venous system from injected fluid, Fuchs injected a 20 per cent solution of sodium bromide into normal kidneys of human cadavers of different ages, as fresh as possible. The injections were watched fluoroscopically. The passage of the fluid from the pelvis into the venous channels was accurately noted. The same phenomenon was studied by means of the corrosion method, in which celluloid dissolved in acetone was injected into the ureter until the mass appeared at the stump of the renal vein. By this method it was shown that the veins were filled by extravasation from the fornices calices. In spite of these observations, it was not clear whether the fluid that left the pelvis at the fornix calices actually entered the surrounding vein stems, and much less clear why this should be the case. Answers to these questions were obtained by further and more minute study of the anatomic relations of the venous system of the kidney. It was found that an artificial perivenous space was created when the veins were forced away from the adjacent renal parenchyma by the extravasated fluid from the ruptured fornix calices. This forceful separation of the vein stem from the parenchyma caused stretching and rupture of the many small venules emerging from the parenchyma to enter the veins. These ruptured venules thus permitted direct communication for the passage of the extravasated fluid from the perivenous spaces into the veins. It is probable that other forms of extravasation, such as subcapsular and sinus-hilar extravasations, which are considerably less frequent than pyelovenous backflow, also result from the rupture of small vessels leading to the various types of veins found in close relationship with the renal pelvis. A number of investigators have attributed pyelovenous backflow to direct penetration of the papillary duct openings of the

papillae. Fuchs, although unable to demonstrate this himself, admitted its possibility in rare instances and then only at a very high pressure. The pressure at which pyelovenous backflow occurs and whether or not such pressures occur spontaneously are of significance. It is shown that in renal colic there is an increase in intrapelvic pressure of the kidneys and that this pressure is of the same nature and actually exceeds that produced during pyelographic filling of the pelvis. The question is whether these higher pressures cause pyelovenous backflow. There are two ways by which it may be shown when pyelovenous backflow occurs in human beings: direct observation by pyelography and the reaction of the organism to increases in pressure in the renal pelvis due to artificial or spontaneous causes. If pyelographic injections are done carefully, they are stopped as soon as the patient complains of pain. The abnormal shadows sometimes seen about the calices in pyelograms represent the initial stages and not the actual pyelovenous backflow, as studied experimentally. Of more practical significance is the greater pressure produced in the renal pelvis during attacks of colic. In such attacks symptoms of injection are common. Fuchs stated: "The septic fever curve in the temperature course of patients with congestion and infection of the urinary passages should always be considered as the clinical expression of pyelovenous backflow waves." Attention is called to the fact that rupture of veins occurring in pyelovenous backflow may be the source of hemorrhage in such conditions as intermittent hydronephrosis and colic associated with pelvic or ureteral calculi. It is possible that pyelovenous backflow may open the way for ascending infections of the parenchyma of the kidney.

Surgical Complications.—Schwarz [17] stated that renal complications are among the relatively rare but clinically important sequelae of operations. The four basic forms may be differentiated: (1) disturbances in function; (2) inflammatory, noninfectious diseases; (3) infectious diseases, and (4) the effects of changes in the efferent urinary passages of the kidney. Postoperative disturbances of the function of the kidney are transient, but may also lead to death. They may be produced by inhibitory reflexes which originate in the other kidney or in the bladder. In some of the cases in which the postoperative fatality is sometimes attributed to the shock of the operation, the cause is masked uremia; for this reason, a test of renal function is always made before every major operation. Postoperative, inflammatory, noninfectious diseases of the kidney in the form of simple degeneration, nephrosis or even nephritis are usually attributed to the anesthesia, but in general it may be said that the effect of the anesthesia, especially since chloroform is no longer in common use, is markedly overestimated.

17. Schwarz, Oswald: Postoperative Kidney Complications, Am. J. Surg. **8**: 1206 (June) 1930.

The infectious diseases of the kidney, owing to the frequency of their occurrence, demand by far the greatest amount of consideration. Urethritis, cystitis, ureteritis, pyelitis, pyelonephritis, abscess of the kidney and pyonephrosis are merely different localizations and, under certain conditions, different stages of the same disease process. One sees cases in which the entire urinary tract is actually attacked by the infection. Formerly the colon bacillus was almost exclusively blamed (90 per cent of the cases) as the exciting germ, but more recent investigations have shown that cocci of various types are constantly gaining greater significance in the hematogenic infections, and particularly in the sequelae of operative interventions.

Schwarz expressed the opinion that the indispensable prerequisite for infection of the pelvis of the kidney is motor insufficiency with or without dilatation of the calix-renal-ureter tubule; also that the diagnosis of "chronic pyelitis" as an independent disease picture is always wrong. He stated that the chronic suppuration originating in the pelvis of the kidney is never an independent disease, but always merely a symptom, and that the aim of the diagnosis is to determine what the factors are that prevent this tendency to spontaneous healing of the inflammation and favor chronicity. Two pathologic factors enter into consideration at this point: the dilatation of the renal pelvis mentioned, and the infection of the renal tissue itself. Schwarz expressed the belief that infected residual urine in the pelvis of the kidney is the primary cause of the chronicity of renal pyuria; the second cause is the pyelonephritis. He further stated that every urologic disease having its onset with severe clinical symptoms, including a high temperature and chill, is due either to a metastatic infection of previously formed hydronephrosis or, in most cases, to the development of metastatic cortical abscess in the kidney. As infections of the kidney following surgical intervention are almost always hematogenic-metastatic, one may say that embolic pyelonephritis represents the typical postoperative complication as far as the kidneys are concerned. The sources of the infection are: the infected urinary bladder, from which the kidney may be infected by both an ascending and a metastatic route, every pus focus anywhere in the body and, finally, the intestinal tract.

Severe disease of the kidney may develop under unfavorable conditions from even the most harmless appearing postoperative bacilluria or mild pyuria. According to Schwarz' view, careful control of intestinal motility occupies the center of the stage in all prevention and treatment of infections of the urinary tract from the colon bacillus.

Tuberculosis.—Braasch [18] considered some of the problems that have arisen recently in the diagnosis and treatment of renal tuberculosis.

18. Braasch, W. F.: Tuberculosis of the Kidney, J. Urol. **23**:669 (June) 1930.

Among the common sources of error in the diagnosis of this disease are: confusion of roentgen shadows caused by lithiasis with calcified processes of tuberculosis, failure of clinical differentiation of pyelonephritis and tuberculosis, overlooking tuberculosis as the primary cause in some cases of hydronephrosis, confusion of granuloma in the bladder secondary to tuberculosis with malignant tumor, failure to appreciate the significance of slight pyuria which may occur without any other clinical evidence in early renal tuberculosis, and the incorrect interpretation of the results of inoculation of guinea-pigs.

Probably the most refined test available in the diagnosis of renal tuberculosis is inoculation of guinea-pigs. Cases have been reported with positive results from the inoculation of guinea-pigs with the urine from supposedly normal kidneys. In 1924, Scholl and Braasch reviewed the records of a small group of patients who had been operated on for supposed unilateral renal tuberculosis and inoculations of guinea-pigs with urine collected from both kidneys had been made. A positive report concerning the supposedly well kidney had been obtained in a number of cases, and it was inferred that many of these patients might have had bilateral tuberculosis. Several years later tests were done in 109 cases, including the 18 or 20 previously studied. Although the inoculation of guinea-pigs made with the urine from the supposedly normal kidney again gave positive results in many cases, it was found that most of the patients were alive and well three or more years after operation and that many of them gave negative results on urinalysis. It was evident that the positive reports from the normal kidney were caused by regurgitation of the bacillus of tuberculosis from the bladder into the atonic lower portion of the ureter on the normal side. After nephrectomy the bacillus persists in the urine from the bladder and regurgitates into the normal ureter for a considerable length of time. Cases have been observed in which a tuberculous kidney was removed, and five years later inoculation of guinea-pigs with the urine from the remaining kidney, which was otherwise normal, gave positive results. The value of the differential renal functional test is another factor in diagnosis emphasized by certain observers. It has been claimed that a definite lesion could not be present in the kidney without causing retardation and diminution of the return of indigo carmine (sodium indigotindisulphonas). It has been Braasch's experience with a divided functional test that although it is often of diagnostic value, there are so many factors involved in the excretion of the dye, the time of appearance and the intensity of color, that the test is frequently inexact and misleading. It is not unusual for the secretion of phenolsulphonphthalein or methylene blue (methylthionine chloride, U.S.P.) to be retarded fifteen or twenty minutes on both sides, in spite of the fact that the blood urea is normal.

It has been stated recently that American urologists use urography too much in diagnosis, particularly in renal tuberculosis. It has also been said that urography is seldom necessary to diagnosis and that it is dangerous when employed in renal tuberculosis. In the hundreds of cases of renal tuberculosis observed at the Mayo Clinic in which urography was employed, no serious harm was done. Urography may prove to be the only means of arriving at a positive diagnosis in the presence of the following conditions: (1) early lesions and small circumscribed areas; (2) tuberculosis confined to one kidney and positive results from the inoculation of guinea-pigs with the urine of the other kidney; (3) differentiation of ureterectasis that is secondary to ascending ureteritis and that occurring with pyelonephritis; (4) identification of doubtful renal shadows; (5) differentiation of pyelonephritis and tuberculosis, and (6) determination of the cause of a few pus cells recovered from the supposedly normal kidney. Although occasionally the pelvic outline is normal, it can be stated that a negative pyelogram will exclude tuberculosis in fully 90 per cent of cases.

Although nephrectomy is usually contraindicated in cases of bilateral tuberculosis, it may be considered occasionally if there is excessive pain, hematuria or acute sepsis in one kidney and if the other side is only slightly affected. Although nephrectomy is not advisable without positive indications, the removal of an occluded kidney apparently relieves such symptoms as dull lumbar pain or vesical irritation, and the patient's general condition improves.

Another problem frequently presents itself in the treatment of patients who continue to have dysuria and frequency several years after nephrectomy. Braasch recently reviewed sixty-five cases in which nephrectomy had been performed between five and fifteen years previously. These patients had had advanced secondary ulcerative cystitis with a markedly reduced capacity of the bladder. Within five years after operation there was a mortality of 37 per cent, somewhat higher than the average. When nephrectomy is performed soon after the onset of infection and before the bladder becomes too involved, the results are much better than in cases in which the duration averages five or six years. The fact that 30 per cent of a group of patients with advanced cystitis and contraction recovered shows to what extent the diseased bladder can recuperate.

Reference is made to a syndrome, similar to that of traumatic shock, which has been observed in several cases following nephrectomy for renal tuberculosis. In two cases, the suprarenal gland was removed with the kidney, and in the other cases it may have been injured. This might explain some of the symptoms, which were suggestive of acute suprarenal insufficiency. The condition was characterized by a sudden drop in blood pressure and extreme prostration, followed by death in

from twenty-four to thirty-six hours. In case the suprarenal gland is removed, steps should be taken to overcome possible insufficiency of epinephrine.

Kretschmer [19] reported 221 cases in which he had observed the patients; 43.5 per cent had had some sort of an operation; 42 of the patients (47.7 per cent) had had an operation for a tuberculous disease. The largest number of cases occurring in any one decade was 73, the ages ranging between 20 and 29. More than half the cases (56 per cent) occurred in patients between 20 and 39 years of age. Kretschmer referred to Wildbolz' report of 245 cases in which bilateral renal tuberculosis was found in 12 per cent of the series, to Brongersma's report of 14 per cent, and to Braasch's 16 bilateral cases in his series of 532 (3 per cent). The records of 180 cases were available, in 35.5 per cent of which there was evidence of involvement of the lungs. Thirty-nine of 123 males had lesions involving the genital tract, that is, of the prostate gland and vesicles, and 26 of these also had lesions of the epididymis. In 121 cases (54.7 per cent) the symptoms had been present for one year. In the next largest number symptoms had been present for two years; there were 33 in this group. Therefore, in 154 cases (69.6 per cent), symptoms had been present for two years before the patients came under observation and were given the correct diagnosis and treatment. Frequency of urination was present in 184 cases (83.2 per cent). Nocturia was present in 166 cases. Pus was present in 201 cases (90.9 per cent). In 194 cases (87.7 per cent) the bacillus of tuberculosis was demonstrated by smear, by inoculation of guinea-pigs, or by both.

Hegedüs [20] stated that the success of renal decapsulation for curing chronic nephritis, as proposed by Edebohls, has been doubtful, but that some good results have been achieved in cases of associated oliguria and anuria in pyelonephritis, of which the following case is an example. A right tuberculous kidney was removed from a youth aged 19 years. Convalescence was uneventful, and he was dismissed from observation on the eighteenth day. Three months later he reported diminishing urinary output. Catheterization showed the bladder to be empty. He had moderate fever and no appetite, and he complained of severe headache and nausea. The nonprotein nitrogen content was 41 mg. Examination did not reveal mechanical obstruction of the left ureter. A ureteral catheter was passed into the pelvis and left in place for six hours. The pelvis was lavaged but without success. After anuria for twenty-four hours, decapsulation was carried out under intercostal anesthesia

19. Kretschmer, H. L.: Tuberculosis of the Kidney, Am. J. Surg. **9**:221 (Aug.) 1930.

20. Hegedüs, Karl: Nephrektomie wegen rechtsseitiger Nierentuberkulose, Ztschr. f. Urol. **23**:847, 1929.

with procaine hydrochloride. The kidney was twice the normal size, its capsule was stretched and it was dark brown and congested. Examination did not reveal a lesion. The patient received 500 cc. of a 4 per cent solution of dextrose immediately after the operation. The bladder was catheterized forty-five minutes later, and 30 cc. of cloudy urine was obtained. Bacteriologic examination continually revealed pus and colon bacilli. In twelve hours 350 cc. of urine was secreted, and the blood pressure dropped to normal. The patient made a good recovery. After the fifth day the output of urine increased to 1,000 cc. in twenty-four hours. The bacillus of tuberculosis was not found, and tests on animals were negative. Three weeks after operation indigo carmine appeared on functional test in six minutes, and nonprotein nitrogen had dropped to 24.2 mg. Three and a half months after operation the patient was in excellent health and had gained considerable weight. Indigo carmine appeared in four minutes, and nonprotein nitrogen was 25.09 mg.

Crenshaw [21] stated that calcification in tuberculous lesions of the lymph nodes, the prostate gland, the kidney and other organs is customarily accepted as indicative that the diseased region is walled off and that immunity is well established, especially in that region. In a period of nineteen years a diagnosis of renal tuberculosis was made in approximately 1,817 cases at the Mayo Clinic; there was roentgen evidence of definite calcification in the kidney in 131 of these (7.1 per cent). The diagnosis was based on shadows in the roentgenogram coincident with cystoscopic or laboratory evidence of tuberculosis, such as the finding of bacilli, positive results of inoculation of guinea-pigs, the characteristic pyelogram, the usual cystitis, nodules in the genitalia or a functionless occluded ureter. The types of calcification seen in the roentgenogram were multiple, scattered small areas, single or localized areas 1 cm. or more in diameter, and large, irregular, diffuse areas, involving either a large portion or the entire kidney. In the first group the small scattered areas are generally caused by deposits of lime. They are occasionally seen singly, and appear as elongated, irregular, faint streaks, or as multiple punctate areas, scattered over a large portion of the kidney, usually in one of the poles. Unless the renal area in the roentgenogram is carefully examined, such areas may easily be overlooked. The second group is the type most easily confused with stone. The shadows are usually of several varieties: a shadow of irregular outline, with a consistence dimmer than that seen with renal stone and varying in size from 1 to 4 cm.; a shadow characterized by great irregularity in its consistence and outline, somewhat resembling filigree work, and definite shadows with a density and contour suggestive of stone.

21. Crenshaw, J. L.: Renal Tuberculosis with Calcification, J. Urol. **23**:515 (May) 1930.

The size of the shadow does not indicate the extent of the tuberculous lesion. A shadow only 1 or 2 cm. in diameter may be present in a tuberculous lesion and involve the entire pole or even the complete kidney. The third group is characterized by large, regular, round shadows of variable density in their different portions. Shadows caused by complete caseation of the kidney may assume the outline of a complete cast of the kidney and are usually irregularly lobulated. The shadow may vary in density in different portions of the kidney; some are so dim as to be scarcely discernible, whereas others are definitely outlined. Occasionally, with complete or extensive calcification, the calcium deposit may be so slight that an accentuated normal renal outline appears in the roentgenogram, and it may be difficult to determine whether it is the shadow of an actual lesion. Renal tuberculosis with calcification may be distinguished from renal calculi by certain signs: If the condition under consideration is due to the presence of renal calculi, evidence of cortical necrosis is not seen in the pyelogram; the shadow of the stone is included in the calices rather than in the cortex; the vesical changes that are characteristic of tuberculosis are absent, and stained smears and inoculation of guinea-pigs give results that are negative for tuberculosis.

In this group of 131 cases of renal tuberculosis with roentgen evidence of calcification, nephrectomy was performed in 82, and medical treatment was given in 49. There were 99 male and 32 female patients. The average age for the group was 41.39 years. The average age of all the patients with renal tuberculosis, with and without calcification, was 35.9 years. In 28 cases (22 per cent) urinary frequency or any inflammatory changes in the mucosa of the bladder that would suggest renal tuberculosis were not present. Of 113 cases, calcification occurred in the right kidney in 49 and in the left kidney in 55; it was bilateral in 9. In several cases there was calcification in the ureter and in the prostate gland. Adding the cases in which the patients were practically well to those in which the patients improved, the general health was greatly improved in 34 (85 per cent) of 40 patients treated by surgical means, and in 7 (58 per cent) of 12 treated medically. The condition of the bladder was greatly improved in 31 (78 per cent) of the 40 patients who received surgical treatment, and in 8 (67 per cent) of those who received medical treatment. The mortality is the same in cases with calcification as in cases without calcification. In general, mortality and longevity are more favorable when nephrectomy is performed than when medical treatment is given.

The diagnosis is poor in cases of active pulmonary tuberculosis in which treatment is medical. With total calcification and a normal bladder, the prognosis is good with either surgical or medical treatment. Nephrectomy should be performed in cases of renal tuberculosis with

calcification as in cases without calcification, except in those in which there is quiescent total calcification coincident with a normal bladder.

Pyelonephritis.—Parmenter, Foord and Leutenegger [22] reported three cases of this condition. In these three nonsurgical cases treatment by urinary antiseptics of various kinds and by pelvic lavage was carried out, but the patients continued to have persistent symptoms and cloudy urine. The medical treatment for gonococcic infection of the kidney is unsatisfactory whether this treatment is given by mouth or topically, such as by lavage of the renal pelvis.

Mathé [23] stated that the internist and general surgeon often confuse pyelonephritis with influenza and various abdominal lesions. The distinguishing feature in its distinction lies in a careful urinalysis, which should include culture of the urine in order to ascertain the true nature of infection, as the colon bacillus will often overgrow and outshadow staphylococcus, streptococcus and other organisms. Early catheterization and drainage in acute pyelitis are advised in all cases in which acute hydronephrosis is suspected of being due to obstruction caused by congestion, the result of inflammatory processes in the ureter and pelvis which lead to greater narrowing of the physiologically constructed portions of the ureter.

Mathé suggested as a modern treatment for chronic pyelonephritis the systematic eradication of all possible foci of infection, the elimination of stasis in the upper and lower parts of the urinary tract, drainage and lavage as a routine procedure, alternating silver nitrate with the penetrating dyes, and the employment of local immunization by the injection of the filtrate directly into the renal pelvis.

Of the 347 patients observed by Mathé over a period of years, 45 were not improved. Thirty of these presented stasis in either the upper or the lower part of the urinary tract which was an unquestionable factor in lowering the resistance of the kidney, making it more susceptible to infection. One hundred fifteen patients improved slightly, improvement consisting of more or less transitory amelioration of symptoms; the urine, however, continued to show infection. Nephrectomy was performed on 15 patients.

Perinephritic Abscess.—Campbell [24] presented a clinical study of eighty-three cases of perinephritic abscess. This disease is of extrarenal or intrarenal origin and in most cases is caused by bacterial metastasis.

---

22. Parmenter, F. J.; Foord, A. G., and Leutenegger, C. J.: Gonococcal Pyelonephritis, J. Urol. **24**:359 (Oct.) 1930.

23. Mathé, C. P.: The Differential Diagnosis and Modern Treatment of Pyelonephritis, J. Urol. **24**:119 (Aug.) 1930.

24. Campbell, M. F.: Perinephritic Abscess, Surg. Gynec. Obst. **51**:674 (Nov.) 1930.

Although the predominant symptoms are fever, pain in the costovertebral angle, leukocytosis and reflex urinary frequency, a lesion other than perirenal abscess may be suggested both subjectively and objectively. With this confusion of symptoms and often meager or indefinite clinical data, the diagnosis is difficult. In a third of the cases in the series, the diagnosis is made only at necropsy. Stereoscopic roentgenography is of special value when it shows obliteration of the margin of the psoas muscle on the side of the abscess or lateral spinal curvature away from the abscess. Moreover, when complicating subphrenic abscess is present, elevation and fixation of the diaphragm, with obliteration of the costophrenic sinus, are diagnostic. Technical urologic examination may not be of aid; in two cases in the series it actually confused the diagnosis. The treatment is surgical drainage, although in rare instances a patient recovers without operation. Complications are common and involve the pulmonary and genito-urinary systems in particular. Of the fifty-four patients operated on for perirenal abscess, eleven died, an operative mortality of 20.4 per cent. It is noteworthy that most of these fatalities were directly due to complications and the surgical treatment thereof rather than to the primary abscess.

Sisk and Wear [25] reported three cases of gonococcal infections of the kidney, ureter and bladder. Johnson and Hill stated that ascending infection to the kidney may occur just as invasion of successive portions of the urethra ocurs against the urinary stream. It has been demonstrated that infection in the renal pelvis from the bladder may occur under certain conditions, and in view of the frequency with which the neck of the bladder is involved in gonorrheal infections, this route of infection merits consideration. Simmon favored the hemic or descending route, and the possibility of infection by this route is recognized when one considers the frequency with which gonococcal bacteremia occurs, the low resistance of the patient and the great virulence of the organisms in many cases.

The similarity of gonococcal cystitis to tuberculous cystitis, although mentioned as early as 1902 by Asch and later by Barney and Buerger, has never been sufficiently emphasized. Of the thirty-two cases reported in the literature as gonococcal infections in the kidney and ureter, the diagnosis is doubtful in all but four. The value of fermentation or serologic tests for confirmatory evidence cannot be questioned, but it is believed that the experienced urologic diagnostician, with the aid of an expert laboratory worker, can accurately diagnose this condition by

25. Sisk, I. R., and Wear, J. B.: Gonococcal Infections of the Kidney, Ureter and Bladder, J. Urol. **23**:639 (June) 1930.

other means. The difficulty in growing the gonococcus on artificial mediums is generally recognized.

Little is known about the treatment of gonococcal infections of the kidneys and bladder. The consensus favors the use of silver salts in the bladder and kidneys.

The prognosis in this type of infection must be guarded. Reaction to treatment begun in the early stages may be satisfactory, but even when the treatment is begun early, recovery may be prolonged and tedious to both patient and surgeon.

Resection.—Herbst and Polkey [26] investigated, experimentally, various types of technic in renal resection. They observed the incidence of hemorrhage, fistulas, atrophy and compensatory hypertrophy, and determined the renal function following resections as evidenced by the excretion of phenolsulphonphthalein.

In thirty-seven dogs the kidney was resected under healthy conditions and without disturbing the opposite kidney. Resection of the kidney reduced the weight and phenolsulphonphthalein function in all cases and at all times. Function decreased approximately in proportion to the loss of secreting renal tissue, even when small amounts were removed.

Resection of small amounts of renal substance did not affect the life or health of the dog and did not cause compensatory hypertrophy of either the resected or the opposite healthy kidney.

Complete atrophy and complete loss of function of the resected kidney did not occur in thirty-four weeks, although there was always some reduction of weight and size, relative atrophy from disuse was never observed.

[Ed. Note.—The observations of Herbst and Polkey are of value in demonstrating that the function of the individual kidney is impaired permanently in direct proportion to the amount of secreting tissue removed. The fact that compensatory hypertrophy does not commence at once either in the partially resected kidney or in the opposite kidney, even when considerable amounts of tissue are removed, is of especial significance and somewhat at variance with the usual impression.

Doubtless, as these authors intimated, there is a definite excess of renal tissue in the body which may be removed up to a certain quantitative amount before the stimulus for compensatory hypertrophy on the part of the remaining renal tissue comes into physiologic activity.]

---

26. Herbst, R. H., and Polkey, H. J.: Renal Resection: An Experimental Study of Postoperative Function, Surg. Gynec. Obst. **51**:213 (Aug.) 1930.

(*To be Continued*)

THE ARCHIVES OF SURGERY is published by the American Medical Association for the advancement of surgery and as a medium of publication for research, clinical observations and experimental work in surgery.

Manuscripts for publication, books for review, and correspondence relating to the editorial management should be sent to Dr. Dean Lewis, Editor-in-Chief, Johns Hopkins Hospital, Baltimore, Md., or to any other member of the Editorial Board. Communications regarding subscriptions, reprints, etc., should be addressed, ARCHIVES OF SURGERY, American Medical Association, 535 North Dearborn Street, Chicago.

Articles are accepted for publication on condition that they are contributed solely to the ARCHIVES OF SURGERY. Manuscripts must be typewritten, preferably double spaced, and the original copy should be submitted. Zinc etchings and halftones of illustrations will be supplied by the Association when the original illustrations warrant.

Footnotes and bibliographies should conform to the style of the Quarterly Cumulative Index Medicus, published by the American Medical Association. This requires, in order given: name of author, title of article, name of periodical, with volume, page, month—day of month if weekly—and year. A complete list of abbreviations for standard periodicals, together with a full discussion of the style of the A. M. A. publications, appears in The Art and Practice of Medical Writing, a comprehensive book on the preparation of medical manuscripts, published by the American Medical Association. Price, $1.50.

Matter appearing in the ARCHIVES OF SURGERY is covered by copyright, but, as a rule, no objection will be made to its reproduction in reputable medical journals, if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the ARCHIVES OF SURGERY, or in any of the other publications issued by the Association, will not be permitted.

Authors will receive one hundred reprints free; additional reprints may be obtained at cost.

The ARCHIVES OF SURGERY is issued monthly. The domestic, annual subscription price (two volumes) is $8.00; Canadian, $8.40; foreign, $8.75, including postage. Single copies, 85 cents.

Checks, etc., should be made payable to the AMERICAN MEDICAL ASSOCIATION.

OTHER PERIODICAL PUBLICATIONS
of the American Medical Association

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION—Weekly. Covers all the medical sciences and matters of general medical interest. Illustrated. Annual subscription price (two volumes): Domestic, $7.00; Canadian, $8.50; foreign, $9.50. Single copies, 25 cents.

ARCHIVES OF INTERNAL MEDICINE—Monthly. Devoted to the publication of advanced, original clinical and laboratory investigations in internal medicine. Illustrated. Annual subscription price (two volumes): Domestic, $5.00; Canadian, $5.40; foreign, $5.75. Single copies, 75 cents.

AMERICAN JOURNAL OF DISEASES OF CHILDREN—Monthly. Presents pediatrics as a medical science and as a social problem. It includes carefully prepared collective abstracts based on recent pediatric literature, abstracts from foreign and domestic literature, book reviews, society transactions, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF NEUROLOGY AND PSYCHIATRY—Monthly. A medium for the presentation of original articles on nervous and mental diseases, with abstracts from foreign and domestic literature, book reviews, society transactions, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY—Monthly. Devoted to advancing the knowledge of and progress in cutaneous diseases and syphilis. Publishes original contributions and full abstracts of the literature on these two subjects, transactions of the important dermatological societies, book reviews, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF OTOLARYNGOLOGY—Monthly. A medium for the presentation of original articles on diseases of the ear, nose and throat, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75. Single copies, 75 cents.

ARCHIVES OF PATHOLOGY—Monthly. A periodical devoted to the publication of original contributions in the field of pathology, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75. Single copies, 75 cents.

ARCHIVES OF OPHTHALMOLOGY—Monthly. Includes original articles on diseases of the eye, abstracts from foreign and domestic literature, book reviews, transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

QUARTERLY CUMULATIVE INDEX MEDICUS—Quarterly. A complete subject and author index to the worth-while current medical literature of the world. Issued four times a year. Second and fourth volumes bound for permanent reference. Subscription price, calendar year: Domestic, $12.00; Canadian, $12.50; foreign, $12.75.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn St. CHICAGO

CONTENTS

PAGE

Recurrence of Varicose Veins Following Injection: A Study of the Pathologic Nature of the Recurrence and a Critical Survey of the Injection Method. Nelson J. Howard, M.D.; C. R. Jackson, A.B., and Edmund J. Mahon, M.D., San Francisco 353

The Formation of Bone Under the Influence of Epithelium of the Urinary Tract. C. B. Huggins, M.D., Chicago .. 377

The Association of Raynaud's Disease with Cerebral Symptoms: Report of a Case with Migraine, Psychoneurotic Symptoms, Transient Hemiplegia and Death. Louis Carp, M.D., New York 409

Tuberculosis of the Stomach: An Analysis of Cases Recently Reviewed. Ralph W. Good, M.D., Cincinnati. 415

The Rôle of the Pyloric Sphincter in the Behavior of Gastric Acidity. Robert Elman, M.D., and A. P. Rowlette, M.D., St. Louis 426

Pyloric Block, with Special Reference to the Musculature, Myenteric Plexus and Lymphatic Vessels. Bayard T. Horton, M.D., Rochester, Minn. 438

Attitudes Associated with Lesions About the Hip Joint. Vernon L. Hart, M.D., Ann Arbor, Mich. 463

Spondylitis Deformans. Samuel Kleinberg, M.D., New York 485

The Effect of Atelectasis on the Pulmonary Blood Volume. Jacob Fine, M.D., and Cecil K. Drinker, M.D., Boston 495

A Review of Urologic Surgery (to be Continued). Albert J. Scholl, M.D., Los Angeles; E. Starr Judd, M.D., Rochester, Minn.; Linwood D. Keyser, M.D., Roanoke, Va.; Gordon S. Foulds, M.D., Toronto, Canada; Jean Verbrugge, M.D., Antwerp, Belgium, and Adolph A. Kutzmann, M.D., Los Angeles 503